Mathematical modelling of the dynamics and control of *Salmonella* on UK pig farms

Thesis submitted in accordance with the requirements of
the University of Liverpool for the degree of Doctor in Philosophy
by
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August 2012

Abstract

The work in this thesis falls into three parts. The first part relates to the time spent with the industry as part of this CASE Studentship, whilst the second and third parts relate to stochastic transmission models and the analysis of interventions imposed upon these models. The second and third parts are linked by a common aim, which is to develop models to understand the dynamics of *Salmonella* transmission on a pig farm and thus identify key drivers of *Salmonella*.

The thesis begins with an assessment and analysis of a Farm Tool Questionnaire that was developed by the industry. A total of 28 farms were visited, had pooled faecal samples taken and completed the Farm Tool Questionnaire. The main aim of this study was to pilot the developed tool and identify any areas that could be modified in order to enhance its usability. Furthermore, the results from the study were used in an attempt to highlight any possible areas of farm management that differ between Platinum farms and non-Platinum farms. It was shown that Platinum farms were likely to adopt a subset of biosecurity practices, which should consequently encourage farms to adopt a range of biosecurity practices rather than focusing on one aspect of biosecurity.

The thesis then turns to the development of mathematical models in order to try and understand how the components of the system interact by using both numerical simulation and mathematical analysis. As farming methods differ considerably between farms, two key forms of unit structure were analysed: a fully slatted unit and a solid floored unit. The models were developed using a semi-stochastic transmission model similar to Xiao et al. [2006] (Y. Xiao, D. Clancy, N. P. French & R. G. Bowers. A semi-stochastic model for *Salmonella* infection in a multi-group herd. *Mathematical Biosciences*, 200(2):214-233, 2006). These were then used to assess any differences in dynamics as a result of farm structure. Finally, both sets of models were analysed in order to identify any possible interventions that could have some form of control on *Salmonella* prevalence at slaughter.

The models showed that the key drivers of *Salmonella* transmission were the amount of bacteria shed and the probability of infection after exposure. As such, interventions focusing on these aspects should be implemented in order to see the most beneficial results. The rate at which infection was able to spread when shedding was high was found to be

of great importance within the various models; indicating that solid flooring is a potential risk factor. Furthermore, as infection was able to spread quickly within the solid-floored unit, the time interval at which cleaning and disinfection were carried out could be of importance. However, this would require further investigation.

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Acknowledgements

I would like to offer my sincere gratitude to my supervisors, Professor Damian Clancy, Dr Robert Christley and Dr Helen Clough for giving me the opportunity to work on this project and enabling me to complete this PhD. I would like to thank them all for the advice and support I have been given.

I would like to thank the Biotechnology and Biological Sciences Research Council (BBSRC) and BPEX for sponsoring me as a PhD student whilst working on this project. I am also grateful to the University of Liverpool for their guidance during my time here. I would also like to thank everyone at BPEX and the Animal Health and Veterinary Laboratories Agency (AHVLA) Weybridge for their support during my placement as part of this CASE studentship; notably Mr Derek Armstrong, Ms Katrin Turvey and Mr A. J. C. Cook.

My special thanks are to my parents, Julie and Alan Berriman, for believing in me and their continued support. I would also like to thank all my colleagues at Leahurst, notably Coll Dawg and Brown Dawg, for getting me through the tough times. My final thanks go to my partner Sarah Lloyd for her support during my studies, and to all family and friends for their encouragement.

In loving memory

of

D. Ronald Harries

List of Abbreviations

AHVLA	Animal Health and Veterinary Laboratories Agency formally known as Veterinary Laboratories Agency (VLA)
BPEX	BPEX, a division of the Agriculture and Horticulture Development Board
cfu	Colony forming units
CI_{95}	95% Confidence interval
DEFRA	Department for Environment, Food and Rural Affairs
EFSA	European Food Safety Authority
ELISA	Enzyme-linked immunosorbent assay
MLC	Meat and Livestock Commission
S. Choleraesuis	*Salmonella enterica* serovar Choleraesuis
S. Typhimurium	*Salmonella enterica* serovar Typhimurium
ZAP	Zoonoses Action Plan
ZNCP	Zoonoses National Control Programme

Chapter 1

Introduction

Studies have shown that the prevalence of *Salmonella* is considerably higher in pigs compared with cattle and sheep (DEFRA [2006a]). With approximately 144,000 cases of human salmonellosis reported in the EU in 2002 (EFSA [2006]), pork, after eggs and poultry, is considered to be a principal source of human food-borne infections. In the United Kingdom (UK), 10,071 confirmed cases of human salmonellosis were reported in 2009 (DEFRA [2011a]), however the true number of human cases of salmonellosis is unknown as it is estimated that 1 case of *Salmonella* is reported for every 5 cases occurring (FSA [2011]). In Denmark, pork (both imported and domestically produced) was estimated to have caused 11.5%-19.1% of human salmonellosis cases in 2004 (Forshell and Wierup [2006]). Further Danish studies have found domestically produced pork to be the second highest source of infection with 9% (CI_{95}: 7.8-10.4%) of cases (Hald et al. [2004]).

Studies investigating *Salmonella* in pigs, cattle and other species have been conducted over a number of years (Davies et al. [2004], Carrique-Mas et al. [2008], Sanchez et al. [2002], Threlfall et al. [2003]), with a number of models describing *Salmonella* dynamics (e.g. Hill et al. [2007] and Xiao et al. [2005]). In this thesis, stochastic models of *Salmo-*

nella transmission within a British pig finishing unit have been created. The aim is to use the developed models to understand the dynamics of *Salmonella* transmission, and thus identify key drivers of *Salmonella*. This information can then be used to investigate control strategies and whether differing farm practices and structures affect *Salmonella* dynamics.

Salmonella is an ever present problem within the food chain, not only in pigs, but also in poultry, cattle and sheep. Numerous studies have been conducted with regard to *Salmonella* infection for all these animal populations. Evidence has shown spatial clustering of *Salmonella* in cattle (Fenton et al. [2008]) and more recently on UK pig farms (Clough et al. [2009]), which could suggest the dynamics of the organism is similar within different animal populations. As the bacteria can be consumed by humans, procedures that minimise the amount of bacteria entering the food chain must be implemented. An increasing problem is the development of antimicrobial resistance in certain serotypes (Carrique-Mas et al. [2008], Threlfall et al. [2000], Threlfall [2002]). In 2004, it was found that there were 2,541 serovars (Popoff et al. [2004]) of *Salmonella*, categorised into two species: *S. enterica* and *S. bongori*. *S. enterica* can be further categorised into six subspecies: *enterica, salamae, arizonae, diarizonae, houtenae* and *indica*. The 1500 or so *S. enterica* subspecies *enterica* contain the non-typhoidal serovars, which cause approximately 99% of *Salmonella* infections in humans (Brenner et al. [2000]). Certain serovars have adapted to a certain species, such as *S. Abortus ovis* in sheep and *S.* Dublin in cattle (Forshell and Wierup [2006]).

1.1 *Salmonella* and pigs

Recent reports of *Salmonella* in pigs in the UK show 26% of meat juice samples were *Salmonella* positive, with the most common serovar *S.* Typhimurium ($\approx$ 70% of incidents; VLA [2007]), which shows very little change from previous studies (Davies et al. [2004]). An abattoir study in 2003 showed 23.4% (CI_{95} 19.9-27.3%; DEFRA [2006a]) of pigs were *Salmonella* positive. Furthermore, ZAP/ZNCP support visits by the VLA found 31 to 24% of samples positive for *Salmonella* spp. between 2005 and 2009 (Warner [2011]). More recently, 2009 saw 42% of meat-juice samples from assured herds (i.e. herds that supply Quality Assured abattoirs) were found to be positive or weak positive using the *Salmonella* ELISA test (see Section 1.1.1.1); compared to 44.7% in 2008 (BPEX [2010b]). The need to reduce *Salmonella* in British pigs was also recognised by the Food Standards Agency (FSA), who set a target to reduce the incidence of positive pigs at slaughter by 50% by 2010 (FSA [2007]). This however appears not to have been achieved as the incidence of *Salmonella* in pigs in 2010 was similar to that found in 2009 (DEFRA [2011b]).

Salmonella can be found on the skin, in the gastro-intestinal system or in the mouth. However, pigs are largely subclinical carriers of *Salmonella* and excrete the bacteria in the faeces sporadically (Lo Fo Wong et al. [2002]), making it harder to identify cases. Previous studies have shown that pigs infected with *S.* Typhimurium remained infected until 34 to 36 weeks of age (Wood et al. [1989]). Stresses such as transportation and handling can increase the number of pigs excreting *Salmonella*, which has the capacity to expose negative pigs to infection. In the abattoir, although *Salmonella* survival can be considerably reduced, it can nevertheless survive during the scalding, singeing and poli-

shing processes [1] (Lo Fo Wong et al. [2002], Swanenburg et al. [2001b], Bolton et al. [2003]).

Although longer lairage[2] time decreases stress levels in pigs (Warriss et al. [1998]), studies have shown that the lairage in pig slaughterhouses acts as a source of contamination for *Salmonella* free herds (Swanenburg et al. [2001a]). It has also been shown that *Salmonella* isolation is significantly increased with increasing time spent in lairage (Morgan et al. [1987]). On the other hand, Craven and Hurst [1982] found the proportion of *Salmonella* positive pigs declined with increasing time spent in lairage. However, Hurd et al. [2001] found a lower isolation of *Salmonella* from lairaged pigs. Conversely, another study by Hurd et al. [2002] showed a significantly higher ($P < 0.001$) prevalence of *S. enterica* at the abattoir compared with on farm (39.9%, 5.3% respectively).

1.1.1 Control programmes

Abattoir studies demonstrating that approximately 25% of finisher pigs may carry *Salmonella* caused the industry to initiate action. With the introduction of the Zoonoses Action Plan (ZAP) by BPEX (together with the Food Standards Agency (FSA) and the Department for Environment, Food and Rural Affairs (DEFRA)) in June 2002, and more recently the Zoonoses National Control Programme (ZNCP) in April 2008, there is now a focus on a whole chain risk based approach to tackling *Salmonella*. The objective of the ZAP *Salmonella* programme was to identify farms where high proportions of pigs test positive (BPEX [2002]). Although this in itself will not reduce *Salmonella* infection in pigs, it will nevertheless highlight farms where problems with *Salmonella* exist. As the ZAP programme failed to achieve its objective, the ZNCP aims to control and reduce the risk

[1] Processes used in pig slaughterhouses to destroy bacteria on the skin and remove hair.
[2] A place in an abattoir for keeping livestock temporarily.

of *Salmonella* in pig meat by targeting every stage of the production chain (BPEX [2009]).

Under ZAP, farms were allocated a ZAP level, in relation to the number of positive samples as shown below (Cook and Armstrong [2005]):

- Level 3: $\geq 85\%$ of samples tested positive
- Level 2: $< 85\%$ and $\geq 65\%$ samples positive
- Level 1: $< 65\%$ positive.

Quality Assured (QA) farms are those that supply British Quality Assured Pork (BQAP) abattoirs. ZAP level allocation is extremely important to these QA farms, as a continual presence in level 3 can risk their losing assurance status and the ability to send their pigs to Quality Assured abattoirs, and thus incurring a financial penalty. The allocation of farms to levels was motivated by the Danish *Salmonella* control programme introduced in 1993, adding to the programmes for broiler chickens and layer hens that were already in place (Wegener et al. [2003]). The programme assessed feedstuffs, breeder/multiplier herds and finisher herds among other elements (Krarup [2002]), but was revised in June 2000 after an evaluation. One of the main changes of the revision was the meat-juice cut-off level (from optical density OD% 40 to OD% 20), resulting in a large increase in the number of positive samples (Alban et al. [2002]). The meat-juice sampling is also used in the classification system under ZAP, however ODs are converted to a Sample to Positive ratio (S/P ratio) in classifying antibody status as positive or negative (Armstrong [2003]).

1.1.1.1 *Salmonella* detection method

The meat juice enzyme-linked immunosorbent assays (ELISA) test detects antibodies against group B and C_1 *Salmonella* (Arnold et al. [2005], Armstrong [2003]). This involves freezing a sample of muscle tissue and then allowing it to thaw, which in turn releases tissue fluid containing antibodies. The meat-juice antibody ELISA is used within ZAP/ZNCP as a broad indicator of the level of circulation of *Salmonella* within a herd, rather than as an indicator of individual animal infection. Antibodies are generated in response to recent exposure, with the potential for antibody levels to significantly increase with continuous exposure for an extensive period. If previous exposure was for a limited period, then it is likely that antibody levels would be declining below detection levels by the time of slaughter. Nevertheless, continuous reinfection, particularly if associated with stress, would keep antibody production levels high. Although antibodies do not measure severity of infection, it is the duration and excretion levels that are of more significance for modelling.

1.1.2 Transmission routes

The general consensus is that faecal-oral transmission is a significant route of infection (Hill et al. [2007], Ivanek et al. [2004], Lurette et al. [2008]). Airborne/aerosol transmission is also a possibility in the spread of *Salmonella*, as the bacteria has been shown to be able to contaminate adjacent rooms (Proux et al. [2001]). Although aerosol transmission is a possiblilty, the route is generally ignored within modelling. The fact that *Salmonella* can be shed in the faeces in large numbers; up to 10^7 *S.* Typhimurium g^{-1} faeces (Gutzmann et al. [1976]), would further suggest the faecal-oral route to be predominant.

1.1.3 Procedures to minimise *Salmonella*

Although bacteria cannot completely be eliminated in meat production, procedures can be put into place in order to minimise the risk. *Salmonella* and other such bacteria can cause food-borne disease, and so control processes are applied to the whole production line. Food-borne disease is defined as 'disease due to the consumption of food contaminated with micro-organisms or their toxins' (Armstrong [2001]). Any *Salmonella* found in pork products can be eliminated if the meat is cooked properly. The industry, however, cannot solely rely on consumers to do so, which is a major factor in the requirement of having control procedures in place.

Disinfection of premises and equipment takes place throughout the life cycle of the animals. At the farm level, housing and transport vehicles are disinfected on a regular basis. Similarly, at the abattoir, lairage and all equipment are regularly disinfected. Even though pigs from numerous farms go to the same abattoir, it is usual practice for independent transport and no direct mixing; thus transmission of infection between pigs from differing farms is minimised. Although disinfection takes place (on farm, transport and at the abattoir), studies still show the presence of *Salmonella* after the process, highlighting the inadequacy at present (Magistrali et al. [2008]), however studies are being put in place in order to find methods by which *Salmonella* presence is minimised (Bolton et al. [2003]).

1.2 The structure of the British pig industry

The structure of the pig farming industry is shown in Figure 1.1. Nucleus farms are those that supply multiplier farms with their purebred sows and boars. Multiplier herds produce cross breed animals which produce piglets with the best characteristics, which are then

sold to commercial pig farms for weaning. The number of pigs in the UK has been on the decline over the past few years (-3.7% 2007/2008 (DEFRA [2006b]), however there are approximately 500,000 breeding pigs and 4.5 million finishing pigs in the UK (DEFRA [2009]).

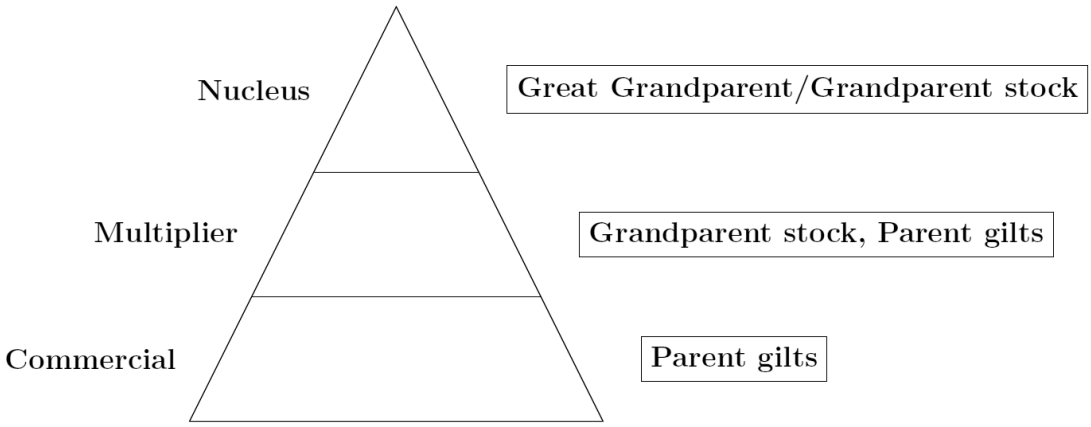

Figure 1.1: Industry Structure (Source Lyth et al. [2003])

Within the commercial group, there are three stages of production; farrowing, weaning and finishing. A farrowing house is a building, often split into rooms with a connecting corridor, with 8 - 20 farrowing pens in them. These pens consist of an area for the sow to lie down for feeding and enough room to stand. The sow is unable to turn in these pens since excessive movement could result in piglet mortality. Within the pen, there is also an area for the piglets with bedding and an infra red lamp in order to control the temperature.

Initially weaners are generally on flat slatted decks, which are often flexible in size (moveable dividers). These are then moved to veranda/kennel style pens or to large weaner pools in straw yards. Finishing houses generally have one aisle with a number of pens

on each side. These pens can be indoor/slatted, veranda/slatted or solid flooring. This is seen in more detail in the codes of practice (DEFRA [2003]), where recommendations for the welfare of pigs concerning housing are given in great detail. The normal number of pigs in each pen in the finishing unit is between 12-24. Pigs within the finishing unit require a temperature of $14 - 20\ ^oC$ for comfort, with a minimum ventilation of around 0.2 m^3 per hour per kilogram metabolic weight, and a maximum of 2.0 m^3/h per kg of pig. The air speed should be approximately 0.1 m/s at pig height (Whittemore [1998]).

1.2.1 Pig breeds

The common definition of a breed is 'a group of animals of common origin that possess certain true breeding distinguishable characteristics that make them different from other members of the species' (Jones [1998]). Commercial pig breeds used in the UK include the Large White, Landrace, Meishan, Duroc, Hampshire and Pietrain. Modern domestic pigs are able to produce 25 to 30 offspring a year from an average of 2 to 3 farrowings. A piglet of birth weight 1.5 kg will increase that weight to approximately 180 kg (i.e. by a factor of 120) in 18 months. In comparison, a 50 kg calf at birth will only increase its birth weight by a factor of about 10 to 500 kg (Lawrence [2002]).

The Large White (or Yorkshire) breed is the most widespread of modern pigs, and was first recognised as a distinct breed in England in 1868 (Jones [1998]). This breed is renowned for having the best growth rate and is beaten only by the Meishan for its litter size. Growth rate may exceed 750g daily from birth to 100kg, producing a carcass with 55-60% lean meat. Puberty is at around 180 days, and litter size is around 11/13 piglets with an average birth weight of approximately 1.25 kg.

The Landrace is a commonly used breed nationally. The original Scandinavian Landrace are quite lean and acceptably prolific, but not especially muscular. In Denmark, for many years the Landrace was selected for bacon production and farmed as a single pure breed, and is perhaps the most famous of all breeds as an example of the success of progency testing and selective breeding. Now, however, its main use is in crossing with the Large White (Whittemore [1998]).

1.2.2 Meat production

In the UK, meat production is aimed at 3 different markets; pork, bacon and heavy hog.

Pork pigs. Approximately 60% of all pigs are pork pigs. Large numbers are sold in markets on a live weight basis, with others sent directly to slaughter houses, with payment received on a dead-weight basis. In all cases the meat is sold fresh and is not cured. Live weights vary from 50 to 55 kg ($\approx$ 4 months of age; light pork pigs) to 70+ kg (about 5 months of age; heavy pork pig or cutter, Lawrence [2002]). Breeds that are relatively small and early maturing, such as the Middle White and Berkshire (Lawrence and Stewart [2008]) are used.

Bacon pigs. Approximately 30% of all pigs are bacon pigs, which are between 85 and 90 kg live weight at 5 to 6 months of age. Nearly all are sold on a dead-weight basis, and the meat is cured (bacon, ham, etc; Lawrence [2002]). These animals are late maturing, such as the Large White, Landrace, Tamworth and Welsh (Lawrence and Stewart [2008]).

Heavy hog or manufacturing pigs. These account for the remaining 10% of pigs

produced in the UK. Most are sold under contract, with payment usually on a dead weight basis. The higher live-weight at slaughter (110 - 120 kg at 6 to 8 months of age) gives bigger carcasses, offering more scope for cutting in different ways. From such a carcass, meat can be cured for bacon and hams, used in sausage, black pudding and pie manufacturing and the excess fat can be trimmed to give lard for cooking (Lawrence [2002]).

1.3 Modelling techniques and history

Models are generally used as a tool to explain how an object will behave. A mathematical model however is an abstract, simplified, mathematical construct related to a part of reality and created for a particular purpose (Bender [2000]). By using mathematical models to describe a system, a more refined and precise description of the system can be provided. By definition, all models are "wrong" in the sense that even the most complex model will make some simplifying assumptions. As such, modelling a problem becomes a trade-off between three important and often conflicting elements: accuracy, transparency and flexibility (Keeling and Rohani [2008]).

1.3.1 The use of mathematics in the study of epidemics

The reason why mathematics is and can be used within the study of disease is highlighted by Bailey [1975], in which he states that, "in the context of endemic disease we require to know more about how the endemic level is related to factors which can be controlled by public health interventions." He also highlights the need for models to assist the decision-making process by enabling us to evaluate the consequences of choosing any alternative strategies available. As such, "mathematical models of the dynamics of a communicable disease can have direct bearing on the choice of an immunization programme, the optimal allocation of scarce resources, or the best combination of control or eradication

techniques."

The mathematical study of disease has become ever more popular in recent history, with numerous publications in the area emerging historically and more recently (Kermack and McKendrick [1927], Daley and Gani [1999], Hethcote [2000], Andersson and Britton [2000], Diekmann and Heesterbeek [2000]). An early high profile example of epidemic modelling is the deterministic SIR model of Kermack and McKendrick [1927], where SIR describes the flow pattern between the categories during an epidemic. Thus an individual is first susceptible (S), then can become infected (I) and is then recovered/removed (R) from the system. Other acronyms of epidemiological models include SEIR, SIRS and SIS (where E describes a latent period). An important parameter in most epidemiology models is the basic reproduction number R_0, defined as the average number of secondary infections produced when one infected individual is introduced into a host population when everyone is susceptible (for example, Hethcote [2000]). In deterministic models, there is initial exponential spread when $R_0 > 1$, but the disease becomes extinct when $R_0 < 1$. As such, R_0 is considered to be the threshold parameter, determining if/when a disease can become an epidemic. However, for this to be true, a large number of susceptibles and infectives are needed. With the existence of a small number of infected individuals, there is a need to take account of 'demographic stochasticity' (Diekmann and Heesterbeek [2000]). As a result, the use of stochastic epidemic models has become more widespread.

1.3.2 Markov chains

Suppose a continuous time stochastic process $\{X(t), t \geq 0\}$ takes on values in the set of non-negative integers. It is said that the process $\{X(t), t \geq 0\}$ is a continuous time

Markov chain if for all $s, t \geq 0$ and non-negative integers $i, j, x(u), 0 \leq u < s$,

$$P\{X(t+s) = j | X(s) = i, X(u) = x(u), 0 \leq u < s\} = P\{X(t+s) = j | X(s) = i\}. \quad (1.1)$$

As such, a continuous time Markov chain is a stochastic process having the Markovian property that the conditional distribution of the future $X(t+s)$ given the present $X(s)$ and the past $X(u)$, $0 \leq u < s$, depends only on the present and is independent of the past (Ross [2007]). If $P\{X(t+s) = j | X(s) = i\}$ is also independent of s, then the continuous time Markov chain is said to have stationary or homogeneous transition probabilities.

Some properties that follow from the definition of a continuous time Markov chain are that each time it enters state i,
(i) the amount of time it spends in that state before making a transition into a different state is exponentially distributed (as the exponential distribution is memoryless) with mean, $1/q_i$, and
(ii) when the process leaves state i, it next enters state j with some probability, P_{ij}, which is independent of the waiting time. Whereby the P_{ij} satisfies:

$$P_{ii} = 0 \quad \forall i,$$
$$\sum_j P_{ij} = 1 \quad \forall i.$$

In other words, a continuous time Markov chain is a stochastic process that moves from state to state in accordance with a discrete time Markov chain, but is such that the amount of time it spends in each state, before proceeding to the next state, is exponentially distributed. Also, the amount of time the process spends in state i, and the next state visited, must be independent random variables (Ross [2007]).

1.3.2.1 The SIRS model

A simple epidemic model is an SIRS (susceptible-infected-recovered-susceptible) model, which is an example of a discrete state-space, continuous-time Markov process (Daley and Gani [1999]). In its simplest form

$$S(t) + I(t) + R(t) = N \quad t \in [0, \infty) \tag{1.2}$$

where $S(t)$ is the number of susceptible, $I(t)$ the number of infective, $R(t)$ the number of recovered/removed individuals and N is the population size. S, I and R take discrete values (i.e. $S, I, R \in \{0,1,2...\text{N}\}$ where N is fixed). At any time t, there are three possibilities of a transition:

$$\begin{array}{lcll} (S,I,R) & \rightarrow & (S-1,I+1,R) & \text{infection with rate } \frac{\beta}{N}SI, \\ (S,I,R) & \rightarrow & (S,I-1,R+1) & \text{recovery with rate } \gamma I, \\ (S,I,R) & \rightarrow & (S+1,I,R-1) & \text{return to susceptibility with rate } \nu R, \end{array}$$

where β, γ and ν are the infection, recovery and return to susceptibility parameters respectively.

1.4 Thesis aims and formation

The aim of this thesis was to adapt previous models of *Salmonella* transmission in a dairy herd (Xiao et al. [2006]) to the context of a pig farm, and use these models to investigate control strategies. The varying structures of pig herds were also considered to assess whether this has any effect on *Salmonella* dynamics. The models were run in MATLAB 7.10 (The MathWorks Inc.,Natick, MA), to give simulations for *Salmonella* dynamics within the finishing stages of a pig unit within the UK.

The structure of the thesis is in 2 parts. Firstly, results and discussion from work

with the industry partner is given. A 6 month period was spent working with BPEX on a number of projects and meetings, with the majority of time spent working on a Farm Risk Assessment Tool, as described in Chapter 2.

The remainder of the thesis shall discuss the various modelling methods and techniques used within previous models of *Salmonella* dynamics in pigs, and within the models presented. A detailed review of the literature was completed in order to justify the various parameter values used within the models (Chapter 4). The following chapters then describe the models of *Salmonella* dynamics within a British pig finishing unit. Chapter 5 details stochastic transmission models describing *Salmonella* dynamics around a slatted-floored unit. This model is then modified in order to describe the dynamics within a solid-floored unit within Chapter 7. Chapters 6 and 8 describe interventions imposed on the slatted-floored and solid-floored unit respectively. The final chapter, Chapter 9, provides a general discussion.

Chapter 2

Evaluation and analysis of a farm assessment questionnaire

As part of this CASE studentship, a period of approximately 6 months was spent within the industry; which included approximately 2 months within the Centre for Epidemiology and Risk Analysis (CERA) group at the AHVLA (Weybridge), working on management and analysis of pig Salmonella data. The remaining 4 months involved working closely with BPEX on the evaluation of the ZNCPig Salmonella Farm Risk Assessment Tool, which included farm visits, laboratory visits, statistical analysis and database development, as detailed below.

2.1 Introduction

Salmonella control on farm is extremely important as *Salmonella* species are the cause of major zoonotic disease. Although *Salmonella* cases in humans reported in England and Wales have been falling in recent years (17,163 in 2001 compared to 9,133 in 2010; HPA [2011]), and the number of cases connected with pork products has been low (estimated to be between 10 and 20% of human infections within the EU; EFSA [2010]), EU legisla-

tion will require all countries to introduce national *Salmonella* control programmes. The Zoonoses National Control Programme (ZNCP) was "introduced in order to safeguard and build on the image of British pig production, and to help ensure that any risk to consumers, however small, is minimised" (BPEX [2010a]). On the basis of their rolling 12 month results, farms are allocated a ZNCP prevalence of total positive plus suspect results, based on an ELISA antibody test. "Platinum pig" awards are given to units with less than 10% average annual *Salmonella* prevalence.

BPEX and the FSA developed a questionnaire (known as the Farm Tool Questionnaire, Appendix A) to assess the control of putative risk factors for *Salmonella* carriage in pigs on farm. As stated by the Farm Tool questionnaire, "the aim is to use established principles to develop the background information and propose audit style questions indexed to the scientific evidence with proposed relative scoring for pig farms for the control of *Salmonella* on farms." BPEX plan continued development of the Farm Tool, with the intention to make it available nationwide. The aim of this study was to pilot the tool on a small number of farms and to evaluate some of its key aspects. This evaluation included assessment of its use in the field, investigation of responses to the Farm Tool and comparison of these against Platinum status and the results of *Salmonella* culture.

2.2 Methods

2.2.1 Farm Tool Questionnaire

The Farm Tool questionnaire (Appendix A) addressed areas such as vaccination policy (13 questions), incoming stock (2 questions), biosecurity (37 questions, split into different sections), management and feeding practice (10 and 12 questions respectively, for each stage

of production) and pest control (10 questions). The Farm Tool questionnaire contains (almost entirely) closed questions, most requiring a binary yes/no response. Information regarding management and feeding practice however, require a more detailed response. BPEX and the FSA developed this tool, and via the use of "established principles", have scored each response to each question. These scores aim to quantify the efficacy of *Salmonella* control on farm. This results in a farm tool score.

2.2.2 Database development

A significant part of this project was development of a database for long term management of the Farm Tool data by BPEX. An Access database was therefore created, designed and developed with an easy to use interface. A single form was used as the main interface (see Figure 2.1), as this should make data entry easy and efficient for potential users. The database encompasses all questions included within the Farm Tool Questionnaire (Appendix A); additional notes can be added to the sections if necessary. A diagrammatical representation of the database can be seen in Figure 2.2 which highlights the different sections within the Farm Tool Questionnaire.

2.2.3 Farm selection and visits

A total of 28 farms were visited between November 19th 2010 and July 20th 2011. On each farm 20 faecal samples were collected (where possible) and the Farm Tool Questionnaire was completed with the farmer. A sampling protocol was followed to ensure sampling consistency between farms. This included identifying all pens on farm and randomly selecting 20 sampling sites. Different gloves were worn for each sample, which were labelled relating to each sampling site, so any isolates could be located. The faecal samples were sent to AHVLA Winchester within 24 hours of collection and cultured for *Salmonella*.

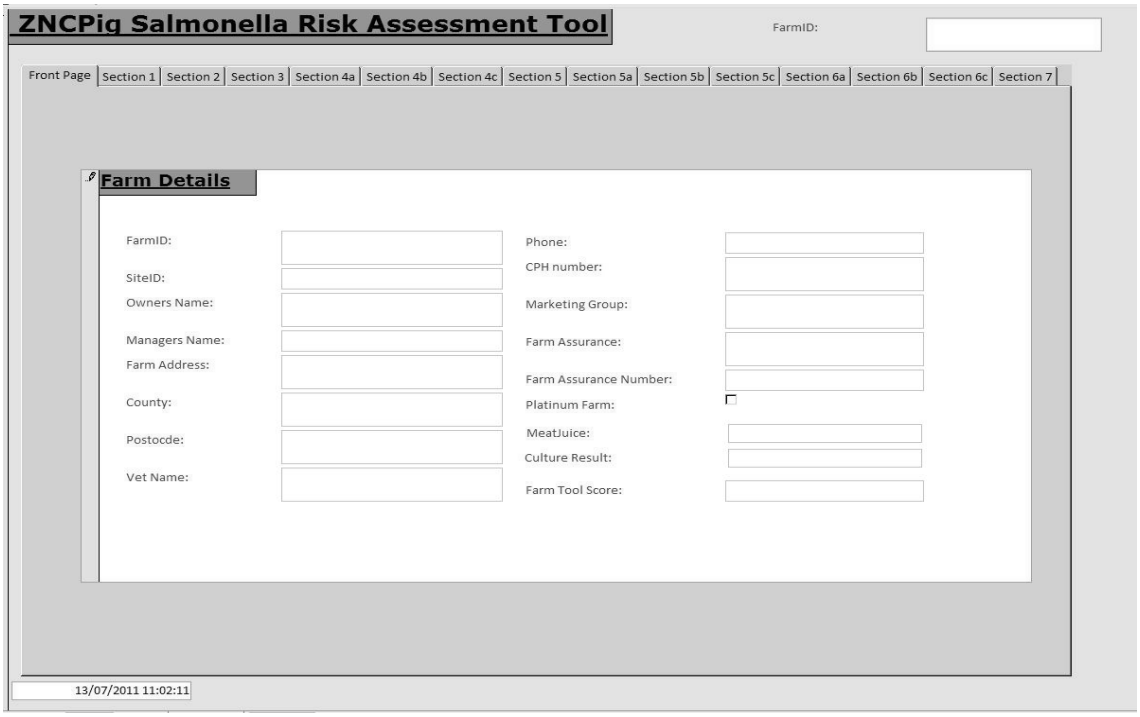

Figure 2.1: Main interface for data entry within the database

Farm sampling was not random, but rather purposive and convenience sampling was undertaken. Specifically, farms were selected that had very high or very low meat juice ELISA results, that had recently lost Platinum status due to a rise in meat juice ELISA results or from among farms who had volunteered to participate.

2.2.4 Statistical analysis

The main aim of the analysis was to identify whether there were any differences between farms, their Farm Tool score, and their meat juice ELISA results (ZNCP). However, the results of statistical analyses presented here should be interpreted with caution. The low number of farms involved in the trial resulted in low statistical power, increasing the probability of type 2 error (failing to detect a true significant effect). In contrast, the large number of statistical tests performed increased the probability of type 1 errors (deciding

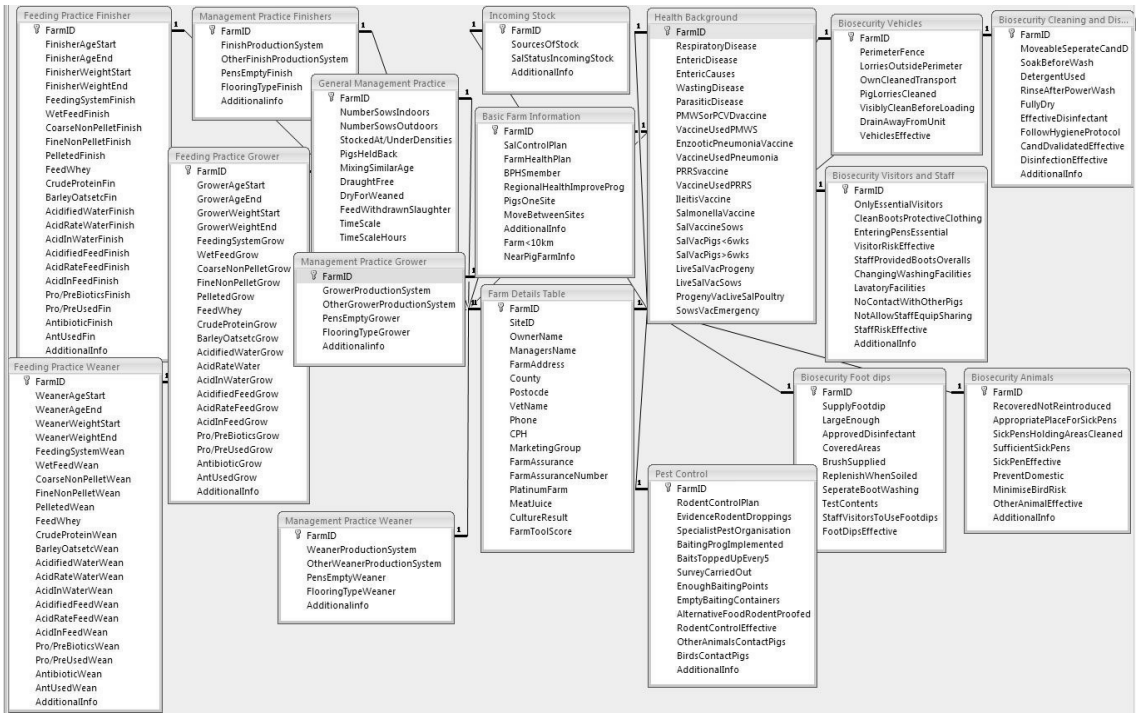

Figure 2.2: A diagrammatical representation of the database

an effect is significant when in fact it is not; i.e. false positives). All statistical analysis was carried out in 'R' (http://www.r-project.org/).

2.2.4.1 Evaluation of ZNCP over time

The first stage of analysis was the evaluation and exploration of ZNCP time series for sampled farms. The ZNCP monthly prevalence over an 18 month period (January 2010 to June 2011) was plotted over time for each farm.

2.2.4.2 Classification of farms

Farms were also classified as Platinum or non-platinum on the basis of the ZNCP score as at January 1st, as requested by BPEX. Principal Component Analysis (PCA) was performed on some sections of the Farm Tool Questionnaire data, in an attempt to highlight

alternative ways of scoring on farm practices. Full definitions and explanations of Principal Component Analysis are given by Everitt and Hothorn [2009] and Manly [2005]. Essentially, PCA aims to describe the variation in the data using new uncorrelated variables in order of their importance, and that describe any variation in the data. These new variables are called principal components. The first principal component should describe the most variability in the data, the second principal component should describe the next most variability in the data and so on. With highly correlated original variables, the best results are obtained, since a large number of variables can be represented by 2/3 principal components (Manly [2005]). The method for PCA generally used in 'R' for numerical accuracy is **prcomp**, where the calculation is done by a singular value decomposition of the centred and scaled data matrix (Crawley [2007]).

PCA score, Platinum status and culture prevalence were compared to identify possible differences in biosecurity practice between Platinum and non-platinum farms, and between farms with differing culture results.

2.2.4.3 Farm Tool responses and culture prevalence

Finally, a comparison of responses from the biosecurity section of the Farm Tool Questionnaire with culture results was completed. In order to investigate the potential impact of each biosecurity measure on the proportion of samples positive on each farm, Wilcoxon Mann-Whitney tests were performed. These tests were selected as data were not normally distributed. The test itself is a non-parametric statistical hypothesis test that is based on the ranks of the observations rather than the original measurements, which is not affected by outliers and does not assume normality (Everitt and Hothorn [2009]).

2.3 Results

2.3.1 Basic farm description

As stated previously, a total of 28 farms were visited, 11 of which were Platinum farms, based on the ZNCP score as at 1st January 2011. Most farms used an all-in, all-out system in some form (as shown in Table 2.1) and generally were reported to have effective cleaning and disinfection. Other systems used included all-in, all-out by pen and all-in, all-out by row, which has been used within all production stages, but mainly by Platinum farms. A continuous flow was rarely adopted within Platinum farms, however $\approx$ 35% of non-platinum farms used some form of continuous flow during finishing. Within a continuous flow system, animals are added to a group (pen) depending on size or age. As a result, animals in many stages (weaners, growers or finishers) can be housed in close proximity to each other.

Table 2.1: Number of farms using each management production system within the study

	Finisher		Grower		Weaner	
	$Plat$[1]	$NPlat$[2]	$Plat$[1]	$NPlat$[2]	$Plat$[1]	$NPlat$[2]
AIAO by building	1	0	2	1	3	2
AIAO by room	3	6	3	8	3	9
AIAO by site	1	2	1	2	3	2
Any AIAO no C& D	1	2	1	1	0	0
Cflow	0	3	0	1	1	0
Cflow no C& D	1	3	0	2	0	0
Other	4	1	4	1	1	1
Unknown	0	0	0	1	0	3

[1] $Plat$: Platinum; [2] $NPlat$: non-platinum
AIAO: All-in, all-out with effective cleaning & disinfection unless otherwise stated.
Cflow: Continuous flow with effective cleaning & disinfection unless otherwise stated.

Finisher pens were generally empty for a shorter period of time (up to 2 days) than grower/weaner pens (1-6+ days; Table 2.2). However, there was not a marked difference

between ZNCP status with regard to this. Furthermore, Table 2.3 appears to highlight a shift in flooring type between weaners and grower/finishers, from slatted flooring to solid flooring. 64% of non-platinum and 54% of Platinum weaners started on slatted flooring compared to 47% and 36% of the corresponding growers/finishers.

For feed, non-platinum farms had a tendency to use predominantly pellets (at least 68%) through all stages of production (Table 2.4). Although a large proportion of Platinum farms used pellets during weaning and growing (63% and 45% respectively), there appeared to be a shift to fine non-pelleted or wet feed, which accounted for 63% of farms during the finishing stage.

Table 2.2: Time pens remain empty for farms within the study

	Finisher		Grower		Weaner	
	Plat	NPlat	Plat	NPlat	Plat	NPlat
< 24 hours	3	4	1	2	0	2
1 - 2 days	5	5	4	5	4	3
3 - 6 days	1	2	3	5	4	5
6+ days	1	4	2	3	3	4
Unknown	1	2	1	2	0	3

Plat: Platinum; NPlat: non-platinum

Table 2.3: Flooring type adopted by farms within the study

	Finisher		Grower		Weaner	
	Plat	NPlat	Plat	NPlat	Plat	NPlat
Fully slatted	3	8	3	6	3	10
Partially slatted	1	0	1	2	3	1
Solid floor: Deep bedding	4	4	4	4	3	3
Solid floor: Some bedding	3	4	2	4	2	0
Outside pens	0	1	0	1	0	1
Unknown	0	0	1	0	0	2

Plat: Platinum; NPlat: non-platinum

Table 2.4: Feeding system adopted by farms within the study

	Finisher		Grower		Weaner	
	Plat	NPlat	Plat	NPlat	Plat	NPlat
Coarse ground non-pellet	0	1	0	3	0	1
Fine ground non-pellet	3	1	3	1	2	1
Pellets	3	11	5	11	7	12
Wet feed, pH < 4.2	2	1	2	1	1	0
Wet feed, pH > 4.2	2	0	0	0	0	0
Unknown	1	1	1	0	1	1

Plat: Platinum; NPlat: non-platinum

2.3.2 ZNCP score and culture prevalence

A total of 24 farms were sampled when visited and therefore have a corresponding culture and ZNCP prevalence.

2.3.2.1 ZNCP prevalence over time

Figure 2.3 presents the ZNCP score over 18 months of selected "typical" Platinum and non-platinum farms, respectively. It can be seen that a typical Platinum farm's ZNCP score consistently remains under 10%, while conversely a non-platinum farm's ZNCP remains considerably higher than this cut off value.

Figure 2.4, however, highlights farms within the study for which ZNCP scores do not follow a similar pattern to the previous farms. The majority of the images (a,c,d) show dramatic changes in ZNCP prevalence between consecutive months. As such, ZNCP can be used to highlight if there is a problem, but does not suggest any answer to its cause.

2.3.2.2 Culture prevalence

The culture prevalence for the majority of Platinum farms remained below 10% and similarly remained higher for the majority of non-platinum farms (Figure 2.5). There were

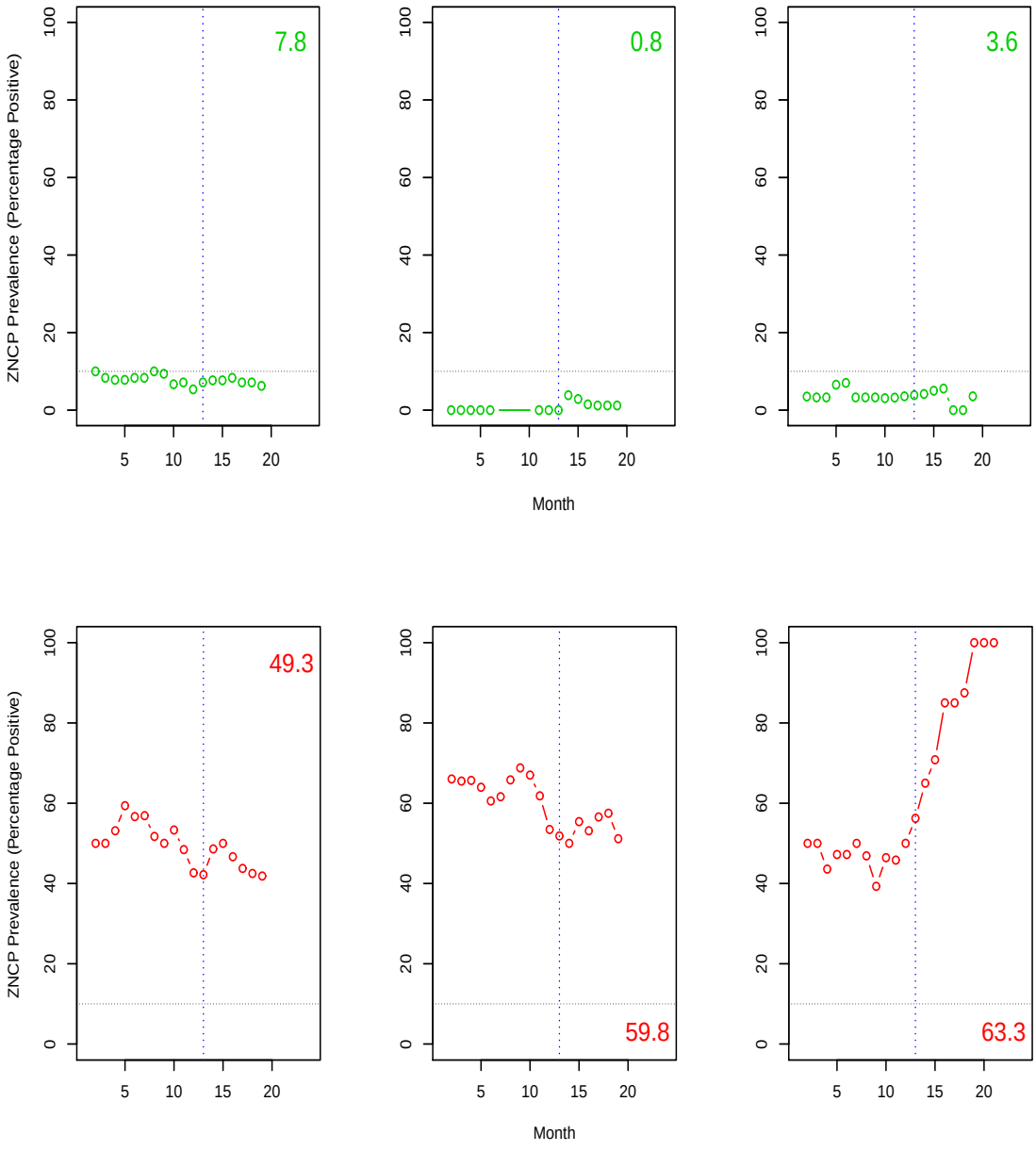

Figure 2.3: Typical ZNCP scores for Platinum farms (top, green) and non-platinum farms (bottom, red). Note: Vertical line - date used for assessment of Platinum status. Horizontal line - 10% cut-off. Mean ZNCP prevalence given in each individual plot; ZNCP scores from February 2010 to July 2011.

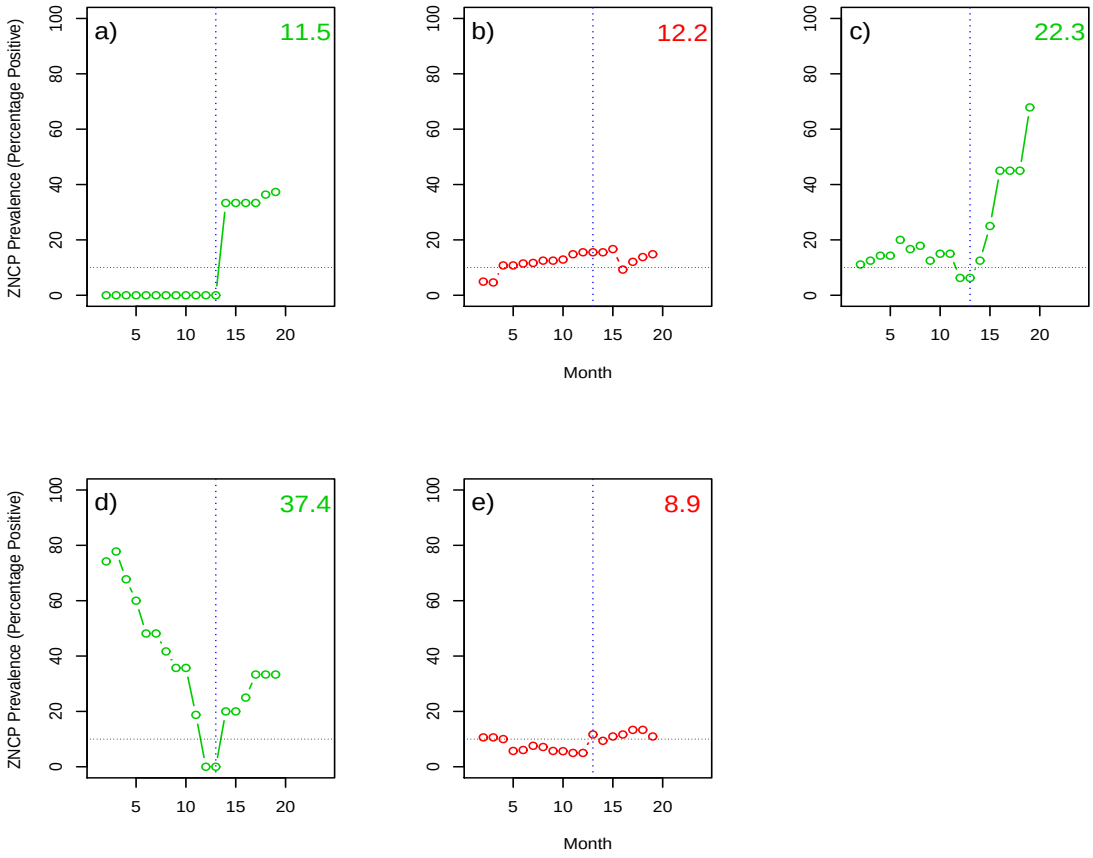

Figure 2.4: ZNCP scores over time for farms sampled. Note: Red graphs - non-platinum farms, Green graphs - Platinum farms. Vertical line - date used for assessment of Platinum status, Horizontal line - 10% cut-off. Mean ZNCP prevalence given in each individual plot; ZNCP scores from February 2010 to July 2011.

however 1 non-platinum and 2 Platinum units that lay outside these respective ranges. The most interesting result was the presence of the new monophasic *Salmonella* variant, which resulted in one of the Platinum units having a high culture prevalence.

2.3.3 Analysis of biosecurity practices

Separate Principal Component Analyses using questions from each individual section of biosecurity from the Farm Tool Questionnaire did not identify any major differences within

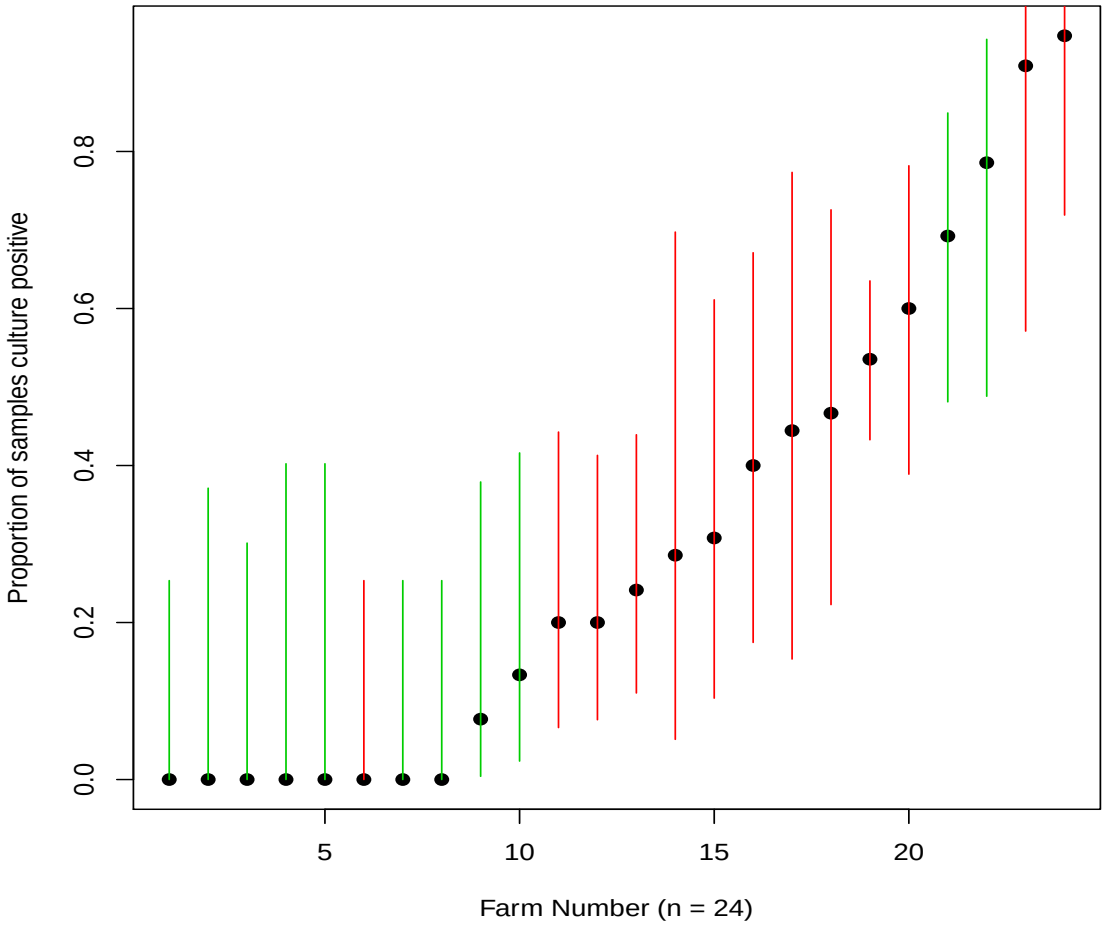

Figure 2.5: Culture results for farms sampled. Note: Black dot - culture prevalence, Lines - 95% Confidence Interval, Green line - Platinum farms, Red line - non-platinum farms

these sections with regard to biosecurity practices between Platinum and non-platinum farms. An additional PCA incorporating all sections of the questions relating to biosecurity appeared to discriminate reasonably well between Platinum and non-platinum farms, using the second Principal Component (Figure 2.6), with Platinum farms tending to score lower on PC2.

By looking at the loadings on each principal component (Table 2.5), a farm was more

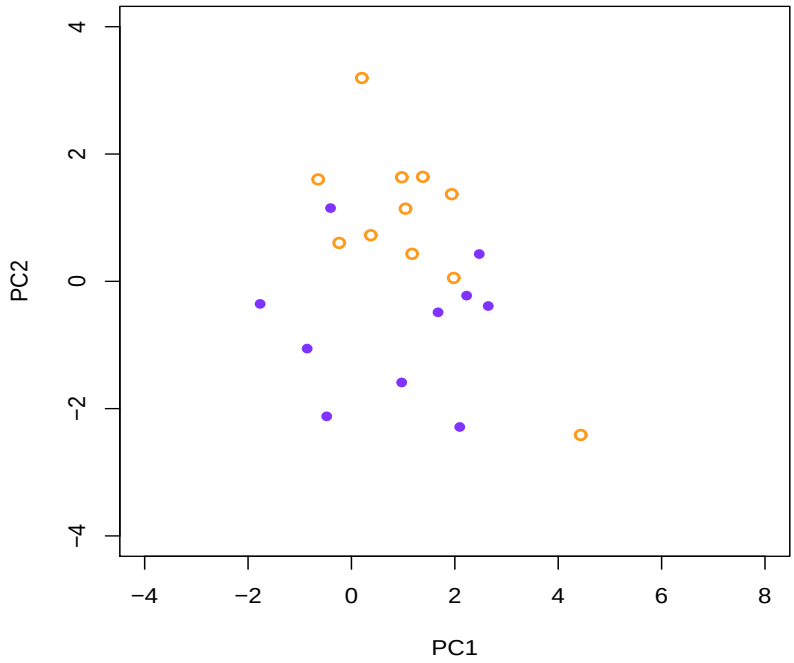

Figure 2.6: Biosecurity Principal Component Analysis highlighting PC1 vs PC2. Note: Purple dots - Platinum, Orange circles - non-platinum.

likely to have a lower (good) score by adopting a combination of good practices relating to staff hygiene, efficient management of sick pigs and thorough cleaning and disinfection practices on farm. This suggests that no single practice was key to attainment of a low score for PC2 but rather, a low PC2 score (and perhaps, therefore, attainment of Platinum status) may be due to adoption of a sufficient subset of these practices.

2.3.4 Association of biosecurity practices and culture results

The apparent impact of individual biosecurity practices upon the proportion of culture results which were positive varied considerably between the practices. For example, there were some areas where performing something actually appeared to result in a higher

Table 2.5: Principal Component 1 and Principal Component 2 loadings within the biosecurity Principal Component Analysis (n = 25)

Category	Question	PC1	PC2
Footdips	4.3.1.1 Supply footdip	−0.303	
	4.3.1.2 Large enough	−0.277	0.135
	4.3.1.3 Approved disinfectant	−0.260	0.138
	4.3.1.4 Covered areas	−0.277	
	4.3.1.5 Brush supplied	−0.298	
	4.3.1.6 Empty when soiled	−0.239	0.140
	4.3.1.7 Separate boot washing	−0.264	
	4.3.1.8 Test contents	−0.295	
	4.3.1.9 Required to use	−0.261	0.147
Visitors	4.3.2.1 Essential visitors		
	4.3.2.2 Clean boots/clothing		
	4.3.2.3 Entering pens essential		−0.179
Staff	4.3.3.1 Overalls and boots		−0.204
	4.3.3.2 Changing and washing		−0.232
	4.3.3.3 Lavatory facilities		−0.129
	4.3.3.4 No contact with other pigs	−0.107	
	4.3.3.5 No staff/equipment sharing	−0.165	−0.101
Sick pigs	4.3.4.1 Recovered not re-introduced		−0.179
	4.3.4.2 Appropriate place		−0.247
	4.3.4.3 Holding areas cleaned		−0.212
	4.3.4.4 Sufficient numbers		−0.298
Other animals	4.3.5.1 Prevent domestic animals		
	4.3.5.2 Minimise bird risk	0.148	
Vehicles	4.3.6.1 Perimeter fence		
	4.3.6.2 Lorries outside perimeter		−0.168
	4.3.6.3 Own cleaned transport	0.104	
	4.3.6.4 Pig lorries cleaned		
	4.3.6.5 Visibly clean	0.118	0.147
	4.3.6.6 Drains away from unit		
C&D	4.3.7.1 Moveable separate C&D	−0.146	−0.243
	4.3.7.2 Soak before washing		−0.242
	4.3.7.3 Use a detergent	−0.203	−0.147
	4.3.7.4 Rinse after power washing	−0.126	−0.194
	4.3.7.5 Rooms to fully dry	−0.159	−0.300
	4.3.7.6 Effective disinfectant	−0.174	−0.194
	4.3.7.7 Follow hygiene protocol	−0.155	−0.263
	4.3.7.8 C&D validated as effective	−0.138	−0.270

(culture) prevalence, for example separate cleaning for moveable cleaning equipment (Figure 2.7). In contrast, using a detergent and visibly clean transport before loading are found to be significantly associated with low culture prevalence (P=0.03 and 0.05 respectively). However, these results should be interpreted with caution due to the limited number of farms included in the analysis. As such, rather than a true indication of significance, the results should be taken as a suggestion that the variables are potentially of more importance, which could be evaluated in future studies.

2.3.5 Qualitative analysis of Risk Assessment Tool scoring system

Due to the different management practices adopted by farms, there were problems when attempting to compare risk tool scores. This was particularly evident when comparing weaner to finisher farms and grower to finisher farms; in such farms, best practice will not necessarily result in the highest score (see Table 2.6). In this example, a mediocre farm encompassing all stages of production can obtain a higher Farm Tool Score than an exceptionally managed farm that only contains finishers.

In an attempt to correct this, it had been proposed to calculate the maximum score of the tool and use a proportion rather than the initial score. However this highlighted other issues with the scoring system. Certain aspects are counter-intuitive, whereby the best practice could receive a lower score, which in turn made calculating a maximum score impractical. For example, with the current scoring system, a closed herd can gain a maximum of 9 additional points, compared to a farm that gets pigs from 1 holding that have been confirmed to be *Salmonella* free that can gain an additional 22 points.

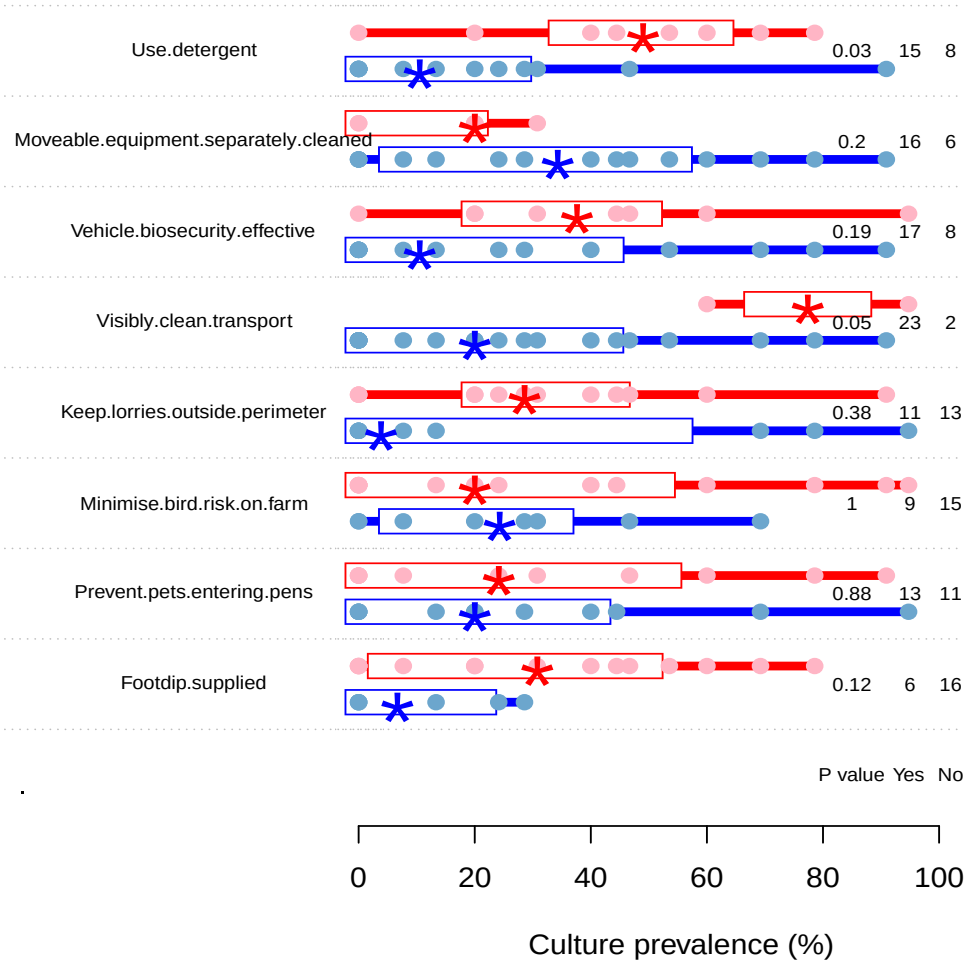

Figure 2.7: A subsection of Wilcoxon Mann-Whitney tests from the biosecurity data. Such farms that answered 'No' to each respective question is represented by a point on the red line and those that answered 'Yes' on the blue line. The mean culture prevalence is highlighted by a star.

2.3.6 Farm Tool Questionnaire modifications

As this was a preliminary trial, there was an opportunity to modify and improve the Farm Tool Questionnaire. Several problems have been highlighted already; the problems with

Table 2.6: A comparison showing the effect varying farm practices have on the farm tool scores

	High quality finishing unit	Average Grower, finisher unit	Average wean to finish unit
Incoming stock	Closed herd	1 site confirmed *Salmonella* free	1-3 sites confirmed *Salmonella* free
Production system	AIAO by site	AIAO by building	AIAO by room
Pens empty	6+ days	3-6 days	3-6 days
Flooring type	Fully slatted	Solid floor with deep bedding	Solid floor with deep bedding
Feed	Wet feed, low pH	Coarse ground, non-pellet	Coarse ground, non-pellet
Farm tool score	61	76	91

AIAO: All-in, all-out (all with effective C & D)

different farm types and with the scoring system.

Certain aspects of responses available within the Farm Tool Questionnaire were problematic. Areas where issues were identified include measurement of the distance from the nearest pig farm. Within the current Farm Tool Questionnaire, a range of less/greater than 10 km was given, which was highlighted by some respondents as being quite wide, however generally a better idea of distance from the closest pig farm was given (i.e. 2 miles), which could be far more useful when analysing risk factors. Furthermore, a number of farms are closed and therefore the *Salmonella* status of incoming pigs needs to have a "Not Applicable" option. A large number of farms gave pelleted feed during all stages of production, which needed to be an option within section 6 of the Farm Tool Questionnaire.

A number of questions within the biosecurity section require more detailed response

categories to be made available. With regard to footdips for example, some farms use other methods which negated the use of footdips, yet result in a low score in this section as all answers are 'No,' despite the methods adopted by farms being potentially as, or more, efficient in terms of biosecurity. For example, rather than using footdips, some farms provided separate boots for each building. It could be argued that this may represent as good, or better, biosecurity than footdips, yet farms undertaking this practice gain no points on the farm tool score.

Similarly, some farms adopted a culling policy for all sick pigs. Despite being likely to be an effective disease control measure, these farms did not have sick pens and as such did not gain points for management of sick animals.

2.4 Discussion

Results from this pilot study revealed some important findings. The main outcome was the potential improvements that could be made to the current Farm Tool Questionnaire, with regard to the structure of the questions and the scoring system used (discussed below). Furthermore, the finding that a Platinum farm was likely to adopt a subset of biosecurity practices could be an important finding as this should encourage farms to adopt a range of biosecurity practices rather than focusing on one aspect of biosecurity, or ignoring biosecurity if they are unable to undertake all relevant practices.

The methodology used to develop the scoring system for the Farm Tool was empirical, however a number of methodologies are available for use within this kind of study. A methodology of scoring system development commonly used is factor analysis (FA) as

described by de Vet et al. [2011]. The principle of factor analysis is to cluster items with high correlation into 1 factor and delete items that have no contribution to the factors. This is a similar methodology to the PCA used within this trial. Scoring systems are often used within observational studies (e.g. clinical trials; for example the ordinal and visual analogue scales), which classify something on a scale; for example, lameness on a scale of 1 to 5. However this is highly subjective and as such is highly dependent on an individual's interpretation (Thrusfield [2007]). Although this is different in terms of the scoring system used, the principles can be applied as a large proportion of questions are subject to the respondents observations and opinions.

As mentioned previously, a number of issues were highlighted regarding the structure of questions and the scoring system used. The main issue with the structure of questions arose within the biosecurity section of the tool. Various practices can be applied to the different aspects of biosecurity, thus the use of yes/no (binary) answers may not be appropriate as they are not totally effective. For example, farms that dispose of any sick pigs, and therefore do not require any sick pens, would not be taken into account with the current status; both within the questionnaire and within the current scoring system. With regard to the scoring system, some aspects are scored in a way that seemed counter intuitive. For example, a closed herd received a lower score than a farm that receives confirmed *Salmonella* free animals from other sources. Furthermore, the scoring for biosecurity could be improved, taking more account of improved biosecurity practices, as discussed previously.

The *Salmonella* culturing raised an interesting result with the presence of the "mo-

nophasic" *Salmonella*, which are variants of *Salmonella* Typhimurium (DEFRA [2011a]). Some reported strains of the monophasic *Salmonella* include 1,4,[5],12:i:-, 4,5,12:i:- and 4,12:i:-, with the latter 2 strains being isolated within this study. Monophasic *Salmonella* had previously been found within mainland Europe (cases in France, Germany and Italy for example), but is slowly beginning to re-emerge within the UK (EFSA Panel on Biological Hazards [BIOHAZ]). The finding of these strains within this study further emphasises the need for a focus on investigations with regard to the presence and control of these re-emerging *Salmonella* strains.

This evaluation of the use of the Farm Tool provides suggestions for modification that may enhance the efficacy of the Tool. The results also suggest that a combination of questions in the Tool are associated with Platinum status and that, therefore, the tool could have utility in informing *Salmonella* control.

Chapter 3

Modelling *Salmonella* dynamics in pigs

Some studies concerning the dynamics of *Salmonella* in pigs have been conducted over the last number of years. Although all very different and unique in their own right, certain aspects of each are compelling. A brief summary of key studies is provided below.

3.1 Hill et al. [2007]

A stochastic transmission model for *Salmonella* within a specialist grower-finisher pig herd (pigs introduced at 30 kg and raised to slaughter weight ($\approx$ 95 kg)) was developed. It is assumed that the system was continuously stocked, with pigs entering/leaving the farm on a weekly basis. *Salmonella* infection was related to meat juice ELISA (MJE) test results at slaughter in order to use ZAP data to estimate parameters.

3.1.1 Methodology

A 'typical' grower-finisher farm model was developed with the following attributes: inside production; exclusive grower-finisher farm (i.e. weaners are sourced from other farms) and a continuous system of production. One building was considered within this farm, which was assumed to be divided into two rows separated by a feeding passage. The population

consists of N pigs, divided into n pigs per pen. The model starts when a new batch of weaners were placed in a randomly selected pen (i_w). Any infected weaners within this batch can either infect a previously *Salmonella*-negative herd or increase the burden of *Salmonella* within a positive herd. The status of weaners entering the farm is determined by the status of the supplier (Ω_{BF}, BF = Breeder Farm), which is randomly assigned. The farm may already be infected by previous weaners on farm, and this status (Ω_{GF}, GF = Grower-Finisher) is also randomly assigned.

Pigs are defined by one of four states: susceptible; infected and excreting *Salmonella* (an excretor); infected and non excreting (a carrier) or immune, where carrier and immune pigs do not contribute to infection and are not themselves susceptible. Carriers, however, may contribute to the infection of susceptibles during transport as stress may cause them to re-excrete. Individual pig status in a positive herd is randomly assigned similarly to herd status; for excretor status, weaners are assigned according to the within herd prevalence amongst weaners (P_{WE}). Similarly, excretor status of pigs in other pens is assigned according to the within herd prevalence amongst grower-finisher pigs (P_{GE}). Both P_{WE} and P_{GE} have been estimated from a British observational study (Davies et al. [2002]), using a negative binomial distribution in order to estimate the number of false negatives. A Danish study (Stärk et al. [2002]) was used to estimate the ratio of shedding to carrier pigs (P_{GC}).

As there is a continuous system of production, pigs in pens other than i_W were taken to slaughter *before* the batch of new weaners reach slaughter age, at time T. Each batch of market weight pigs taken off the farm is assumed to be represented by the removal of

one entire pen, done at a constant period, t_R. Finisher pigs in a newly occupied pen are assigned a status in the same manner as weaners, thus the prevalence of infection may be reduced/increased due to the continual removal and addition of pigs to the farm.

3.1.2 Transmission model

The number of susceptible, excretor and carrier pigs in pen i at time t are denoted as $S_i(t), E_i(t)$ and $C_i(t)$ respectively. The primary route of transmission is thought to be the faecal-oral route (airborne transmission is also a possibility but of less importance), which can occur within and between pens (see Figure 3.1).

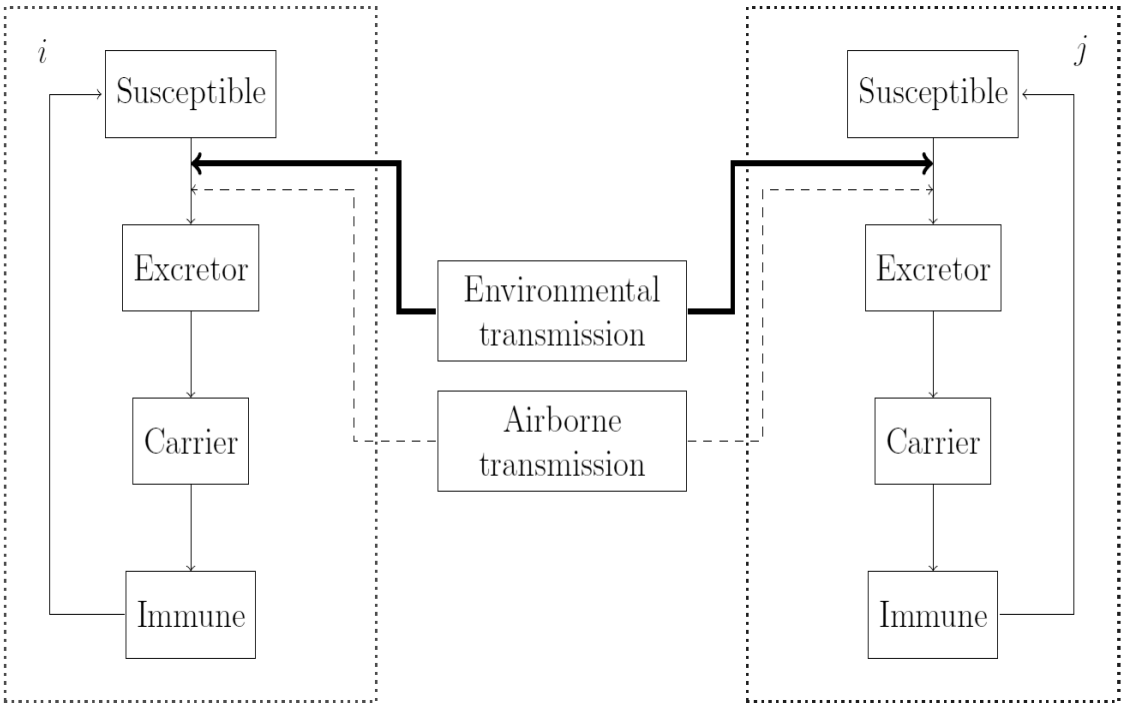

Figure 3.1: Flow diagram of the *Salmonella* transmission model. Reproduced from Fig 1 of Hill et al. [2007].

3.1.3 Model formulation

The probability of infection is determined by the probability of an 'effective contact,' i.e. contact between a susceptible and infective will produce a new case. Each susceptible pig is assumed to have some form of contact (physical, contaminated faeces or airborne) with every excretor on the farm. The probability of an effective contact depends on the distance between pigs, which is represented by the spatial location of the pens containing the susceptible and excreting pigs in question. The probability of a susceptible in pen i becoming infected by excreting pigs in pen j during $[t, t+1]$ is given by: $P_{ij}(t) = 1-(1-p_{ij})^{E_j(t)}$ where p_{ij} is the pen-dependent probability of effective contact. The probability of an effective contact is assumed to be highest between susceptible and excretor pigs within the same pen (p_w). The probability of transmission is assumed to decrease with increasing distance from pen i (i.e. susceptible pen). The way in which p_{ij} varies according to distance between pens i and j is determined by:

$$p_{ij} = \begin{cases} p_w & \text{if } i = j \quad \text{(pigs in same pen)} \\ p_b & \text{if } |j-i| = 1 \text{ and } k_i = k_j \quad \text{(pens adjacent to each other)} \\ p_b/3 & \text{if } 1 < |j-i| < v/2 \text{ and } k_i = k_j \quad \text{(pens in same row, but not adjacent)} \\ p_b/100 & \text{if } k_i \neq k_j \quad \text{(pens in separate rows)} \end{cases}$$

The time step $[t, t+1]$ must be approximately equal to the incubation period, which is stated to be $\approx$ 24-48 hours in pigs. Maximum-likelihood methods were used to estimate the within and between pen probabilities of transmission given effective contact. The likelihood function for $[p_w, p_b]$ is derived by relating *Salmonella* infection with MJE prevalence, and so allowing the use of the ZAP data.

The probability of transition between excreting and carrier states per day ($P_\gamma(t_s)$) is assumed to be dependent on the time since infection, t_s. A Danish longitudinal study

(Kranker et al. [2003]) was used to generate the distribution for the duration of shedding *Salmonella* (γ), which is assumed to be Weibull distributed. The estimated average duration of shedding *Salmonella* was 24.6 days. The length of immunity is assumed to be 10 days beyond the end of the carrier period.

The time taken from infection to MJE positivity is assumed to be Weibull distributed, as is the time that a pig's serological response will remain above the MJE test cut off. The probabilities that an infected pig tests MJE positive t_s days after infection ($P_s(t_s)$) and that serological response falls below the MJE cut off t_d days after seroconversion ($P_d(t_d)$) were estimated using the same method as that for duration of shedding. The average time to a serological response that will test MJE positive is estimated as 58 days and the average time a serological response to infection remains above the cut off as 69.7 days.

3.1.4 Model simulation

The model was simulated using Excel, Visual Basic Editor for Applications (VBA) and @Risk, with 1 day time steps from the time weaners are introduced to pen i_w at t_0 until they reach slaughter age, but are not transported. At each time step, for each susceptible pig, the probability of becoming infected by excretors in their own pen is calculated, and whether they become infected or not (determined by the VBA random number generator). If the pig remains susceptible, the probability of infection by excretors from other pens is calculated. The model loops through each pen until the pig becomes infected or all pigs in the system have been considered for that pig and time step; the next susceptible pig is then considered. Excreting and carrier states also use random number generators to determine whether a transition occurs. At each time step, the model updates the numbers

in each state.

3.1.5 Model output

The prevalence of carriage sharply increases for approximately 50 days after pigs arrive on farm. After this time, the prevalence decreases rapidly, but still consistently remains higher than the prevalence of excretors (Figure 3.2). The average prevalence of excretion for slaughter age pigs is 4.1%, compared to an average carrier prevalence of 11.6% and MJE prevalence of 33.6%. The model predicts an average prevalence of infection at slaughter of 15.7%.

Figure 3.2: Model output showing the mean prevalence of *Salmonella*. Reproduced from Fig 4 of Hill et al. [2007].

3.1.6 Critique

The use of a continuous production system is not assumed within any other study, making this study highly relevant for farms applying this type of methodology. However, this production system is perhaps becoming less common as it has been shown to be a risk factor, both within previous studies (Lo Fo Wong et al. [2004]) and within the BPEX Farm Tool (Chapter 2). The use of the varying probability of infection depending on the location of the various animals is well defined, however the estimates of these values are not well justified. Problems continually arise in modelling with a lack of data, however the logic used in estimating the duration of immunity is well thought through. Serological response has also been modelled, which has not previously been done. Although airborne transmission has been alluded to, the manner in which it is included within the model is unclear. The model variance is said to be large, however this is not shown in the results figure, which would have been useful for interpreting the dynamics.

3.2 Ivanek et al. [2004]

The objective of the study was "to estimate the probability that a random pig leaving an infected finisher farm in Great Britain for slaughter is infected with *Salmonella* Typhimurium." A mathematical model focusing on the transmission of *S.* Typhimurium within an infected grower-finisher pig farm was developed. The results are used to consider which parameters had the most profound impact on *S.* Typhimurium prevalence at the end of the finisher period, when pigs reach slaughter weight.

3.2.1 Methodology

The model aims to describe the transmission dynamics of *S.* Typhimurium on a British grower-finisher farm. The following assumptions were made to simplify the model:

- Grower-finisher farms operate on an all-in-all-out basis, receiving pigs at up to 10 weeks old and rearing them for a further 22 weeks.
- Homogeneous mixing of pigs occurs; pen divisions were not considered.
- A constant number of pigs are present, i.e. no mortality/removals occur prior to slaughter.
- Pigs are the only source of infection.

At any time t, pigs are distributed among four states: susceptible, latent, shedding and carrier (as described in Figure 3.3). The latent stage is the period between infection of a susceptible pig and the onset of shedding *S.* Typhimurium in the faeces. It is also assumed that all infected pigs become carriers at the end of the shedding period and may then eliminate *S.* Typhimurium, thus reverting to full susceptibility. The use of the term carrier is such that a pig is infected but not within the gut contents, but does contribute to final herd prevalence.

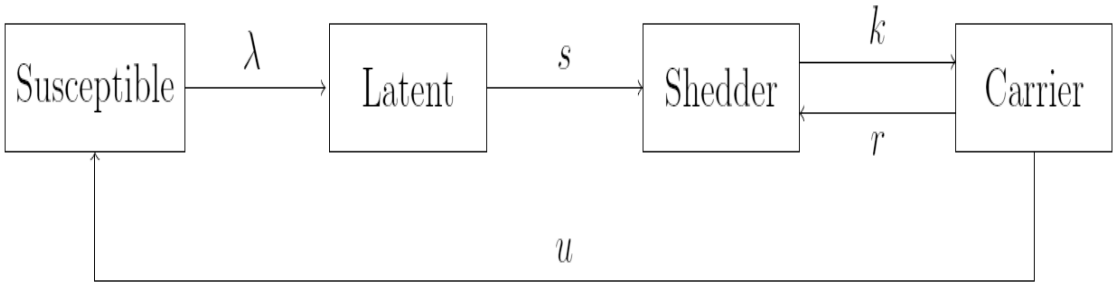

Figure 3.3: Transmission model of *S.* Typhimurium in pigs. Reproduced from Fig 1 of Ivanek et al. [2004].

A differential equation model is used to describe the transitions between the stages. The equations of this model are shown below:

$$\begin{aligned}
\frac{dS(t)}{dt} &= -\lambda(t)S(t) + uC(t) \qquad \text{where } \lambda(t) = \beta I(t), \\
\frac{dL(t)}{dt} &= \lambda(t)S(t) - sL(t), \\
\frac{dI(t)}{dt} &= sL(t) - kI(t) + rC(t), \\
\frac{dC(t)}{dt} &= kI(t) - (u+r)C(t).
\end{aligned}$$

These equations were solved numerically with a time step of half a day in order to estimate the number of pigs in each stage of *S.* Typhimurium infection at time t. To introduce variability into the model, Microsoft Excel and @Risk were used.

3.2.2 Origin of rates and parameters

The rates s, k and u (as shown in Figure 3.3) were estimated from the reciprocal of the duration of the latent, shedding and carrier stages respectively. As there is little data for the duration of *S.* Typhimurium infection in pigs, data for *Salmonella* Choleraesuis infection were used, assuming that the dynamics are similar. The rate at which a pig moves from the latent stage to shedding *S.* Typhimurium (s) was calculated from reports of latent periods (taken to be an average of 2.33 days), with the lognormal distribution being used to describe the variability. The rate at which a pig shedding *S.* Typhimurium becomes a carrier (k) was estimated by calculating the reciprocal of T_S, where T_S was estimated from studies reporting shedding periods, which was taken to be an average of approximately 52 days. Carrier pigs that lose *S.* Typhimurium (rate u) are assumed to become fully susceptible. The duration of this carrier stage is unknown but was estimated by combining the duration of shedding and carrier stages (T_{S+C}), which was taken to be an average of approximately 133 days. Again the lognormal distribution was used to

describe the variability of T_{S+C}. The previous estimate of T_S was subtracted from this value to give an approximation for T_C, the reciprocal of which is the estimate of u.

The rate at which susceptible pigs become infected was determined by the rate at which an infectious pig and susceptible pig make an effective contact (β) and the number of infectious pigs at any time, $I(t)$. In order to estimate this value, output from a Danish workshop was used. One notable part during the explanation of this workshop is the fact that the Danish experts did not include a latent period. It is stated that this is not an issue as the latent period "is usually short, few pigs would be in this stage at any point in time."

The number of pigs per farm comes from an unpublished VLA study of 72 randomly selected British farms, showing a finisher herd size of between 120 and 4,500 (the variability of which is again described by the lognormal distribution between the two values).

3.2.3 Initial conditions of the model

It is assumed that introduced weaners were either susceptible or shedding (i.e. $L(0) = C(0) = 0$), due to the thought that stress associated with transport/mixing would cause any latent/carrier pigs to start shedding. Data from the VLA was used in order to calculate the initial number of shedding pigs ($I(0)$) entering the unit, which was estimated to be $\approx$ 40%.

3.2.4 Model output

The mean prevalence for latent and carrier classes initially increases as the initial assumption is that there were no infected animals at the beginning of the model. However the mean prevalence of shedders decreases over time. The mean within herd prevalence for

an infected grower-finisher farm at the end of the finishing period was 42.7%, with a large proportion of pigs being within the shedder or carrier classes (Figure 3.4); with prevalences of 21.0% and 20.9% respectively. During sensitivity analysis, values for the rate at which a carrier pig resumes shedding, the duration of shedding and the probability of effective contact had the largest impact on the model output.

Figure 3.4: Model output showing the mean prevalence of *Salmonella* infected pigs. Reproduced from Fig 2 of Ivanek et al. [2004].

3.2.5 Critique

Clearly all models have various assumptions in order to make the mathematics manageable. However, this model assumes no pen divisions, which is a large assumption to make, since most farms will have some form of division between groups of animals. As

the duration of the latent class is so small, its use within the model is quite possibly futile, since it has very little effect. One of the key aspects of the model is the inclusion of a transition from the carrier to shedder class, although the transition is initially not included, the effects of this transition are shown within a sensitivity analysis. A hard part of modelling is to estimate the rate of infection, however the study does go some way in attempting to estimate this parameter effectively. The initial conditions of the model appear to be well justified, although the methodology of generating the initial proportion of shedding animals is hard to follow. The mean prevalence was found to be 42.7%, which seemed to be quite high compared to on-farm studies. This however is not surprising due to the long duration animals remain a shedder and carrier, 52 and 85 days respectively.

3.3 Lurette et al. [2008]

A model of *Salmonella* spread within a farrow-to-finish pig herd is developed. A stochastic discrete-time model is presented with four mutually exclusive health states: *Salmonella*-free, seronegative shedder, seropositive shedder and seropositive (not shedding) carrier (Figure 3.5). As indirect transmission is thought to be a significant route of transmission the probability of infection depends on the amount of *Salmonella* in the pig's environment (denoted as Q).

3.3.1 Methodology

A mathematical model simulating the population dynamics within a farrow-to-finish herd was coupled with an epidemiological model of *Salmonella* transmission, resulting in a discrete stochastic model with a time step of 1 week. Also, it is well suited to *Salmonella* infection dynamics as no process occurs under a weekly time-step.

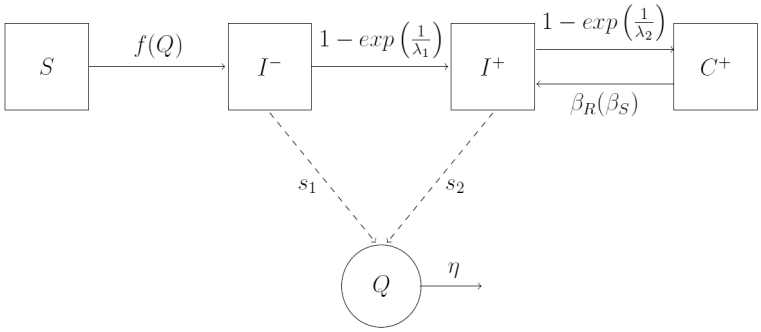

Figure 3.5: Flow diagram of the *Salmonella* transmission model. Reproduced from Fig 1 of Lurette et al. [2008]

3.3.1.1 Population dynamics model

This model includes the entire reproduction cycle of sows and the growth of pigs from birth to the slaughterhouse. Pig growth is split into three stages (rooms); farrowing (S), post-weaning (PW) and finishing (F). The all in/all out system is used (i.e. all pigs in the room leave and enter the next together), which allows each room to be decontaminated between the two batches by a cleaning process followed by a drying period. As growth is variable within a batch, in order to deliver groups with homogeneous weights, several batches can be used. Pigs that are below the expected slaughter weight (and so left behind) remain in a finishing room and are mixed with the following batch (3 weeks younger).

3.3.1.2 *Salmonella* dynamics

The model represents the indirect faecal-oral transmission via free living *Salmonella* in the room. It is assumed that all animals within the room are exposed to the same quantity of *Salmonella*. Within batch transmission occurs due to this contamination whereas between batch transmission occurs via the room due to residual *Salmonella* infectious units in the room after disinfection and/or via the mixing of infected animals from different batches.

The four states that have been adopted are measurable and identified in the literature. Thus the health states are: susceptible (S), shedding (I_-), seropositive shedding (I_+) and seropositive carrying (C_+), with identical transitions for all pigs. The latent period between *Salmonella* ingestion and shedding in the faeces is stated to be less than 24 hours. Due to this the latent period is neglected here as it is assumed to have no effect on the dynamics over the time step of one week. The assumption is made that the seroconversion delay is shorter than the duration of the shedding period. A return to seronegative carrier is also not permitted (i.e. from C_+ to C_-) as pigs would have already reached slaughter weight (average of 178.5 days within the model) before this transition would occur.

3.3.2 Model description

The number of pigs in batch b at time t in growth stage X and health state Y is denoted by $Y^X(t,b)$ where $Y = S, I_-, I_+, C_+$ and $X = S, PW, F$. The probability of infection is dependent on the quantity of *Salmonella* in room r at time t, $Q(t,r)$, and on the number of pigs in batch b in room r at time t, $P^X(t,b)$, and is modelled to represent a dose effect relation.

A fixed degradation rate (η) is applied to Q during each time step. Q is upgraded by the number of infectious units shed by pigs in each room. The shedding of *Salmonella* depends on (i) the growing stage, as finishing pigs and sows produce more faeces than piglets; and (ii) the serological status. The change in Q in room r is represented by

$$Q(t, r(t,b)) = (1-\eta)Q(t-1, r(t,b)) + s_X^1 I_-^X(t,b) + s_X^2 I_+^X(t,b)$$

where $s_X^1 = \pi_X s$ and $s_X^2 = \pi_+ \pi_X s$, with s being the quantity of *Salmonella* shed by a seronegative finishing pig, π_+ the relative shedding of a seropositive compared to a se-

ronegative finishing pig, and π_X the relative shedding of a seronegative pig in growing stage X compared to a seronegative finishing pig. At each disinfecting process, when a batch of pigs leave a growing room, the quantity of *Salmonella* in room r is updated: $Q(t,r) = (1-\nu^r)Q(t-1,r)$, with ν^r the proportion of infectious units eliminated by the disinfecting process in room r.

In batch b, the number of newly infected pigs in growing stage X at time t is drawn by a binomial law. Passive immunity has been shown to be present in piglets at birth, which reduces the susceptibility of piglets. It is therefore assumed that the susceptibility of piglets is reduced during the suckling period compared to other stages. It has been shown however that piglets from seropositive sows can be infected at weaning.

The seroconversion probability is given by $1 - exp(-1/\lambda_1)$, where λ_1 is the average seroconversion delay, which has been shown to range from one to two weeks. The probability to stop shedding *Salmonella* is dependent on the shedding period duration (λ_2), given by $1 - exp(-1/\lambda_2(t))$, where λ_2 is recalculated at each time step (t) to represent variability over time, and hence generate variability between batches. The number of pigs that become seropositive and seropositive carriers at t are drawn by a binomial law.

Transitions between seropositive carrier and shedding states represent the intermittence of shedding, which can occur several times during an animal's lifetime. The probability of shedding reactivation for carrier pigs (β_R) is fixed within the model. As stressful conditions (e.g. weaning) can increase the reactivation of shedding, a different probability, β_S (which is greater than the previous probability) is applied at the weaning of piglets.

3.3.3 Model output

From initially a *Salmonella* free herd, the mean shedding and seropositive prevalence increased over time to 18 and 22% at slaughter respectively (Figure 3.6). The model predicted a high variability in the prevalence of shedding and seropositive pigs at slaughter.

3.3.4 Critique

This study incorporates a large amount of detail at the farm level, since it includes the entire reproduction of sows, through to slaughterhouse delivery. The time step of 1 week appears to be quite large, however there is some justification of this period. Although four health states have been incorporated in order to account for various detection methods, data has not been applied in order to validate the end prevalences. Only indirect transmission is included within the model via the faecal-oral route, which is an over-simplification of the dynamics. However, the amount of bacteria shed is dependent on the age of the animal, which is an important addition to the model.

3.4 Soumpasis and Butler [2009]

This study continued the work of a previous study (Soumpasis and Butler [2008]) by creating a stochastic model for *Salmonella* transmission based on the deterministic model developed previously. The development of the new model followed the same approach used for the deterministic model, whereby a compartment (room) is surrounded by walls and communicates with the rest of the farm with a door and/or windows. As such, a closed system is considered since pigs in the compartment cannot contact pigs from other compartments. The objective of the work is to 'develop a stochastic model that could predict the effect of different compartment sizes and starting conditions of infection (SCI)

Figure 3.6: Model output showing the seroprevalence and shedding prevalence of pigs delivered to slaughter. Reproduced from Fig 3 of Lurette et al. [2008].

on the probability of disease extinctions and the prevalence of the different classes and risk groups of the pigs at time of slaughter.'

3.4.1 Methodology

The compartment/room level of an all-in-all-out pig farm was modelled. A compartment is surrounded by walls and communicates with the rest of the farm with a door and/or windows. It can therefore be thought as a closed/semi-closed system since pigs cannot contact any pig in a different compartment, but can have *Salmonella* introduced by vectors, humans or food.

Within the model, two syndromes were modelled: a high propagation syndrome with high infectious pigs and a low propagation syndrome with low infectious pigs. Pigs can therefore be classed as susceptible (S), high infectious (HI), low infectious (LI), carriers (C), whereby pigs carry the pathogen in internal organs without shedding, and immune (Im), which is represented in Figure 3.7. The reason for this differentiation between HI and LI comes from a study by Fedorka-Cray et al. [1994], which identifies this second disease syndrome, which is subclinical and thus may be important in establishing a carrier state. In order to model the different effect of these 2 classes, a reduced transmitability factor ϵ was introduced, which reflects the reduction in the transmission parameter β for LI pigs relative to HI pigs, where β incorporates the rate of contact between susceptible and infectious individuals, the probability of transmission, and a combination of epidemiological, environmental and other factors that affect transmission rates. In order to model which syndrome is triggered, the environmental load of bacteria was modelled indirectly, by introducing the infectious equivalent (IE), which represents the combination of HI and

LI pigs as a percentage of the total population (N) of the compartment,

$$IE = \frac{HI + \epsilon LI}{N}.$$

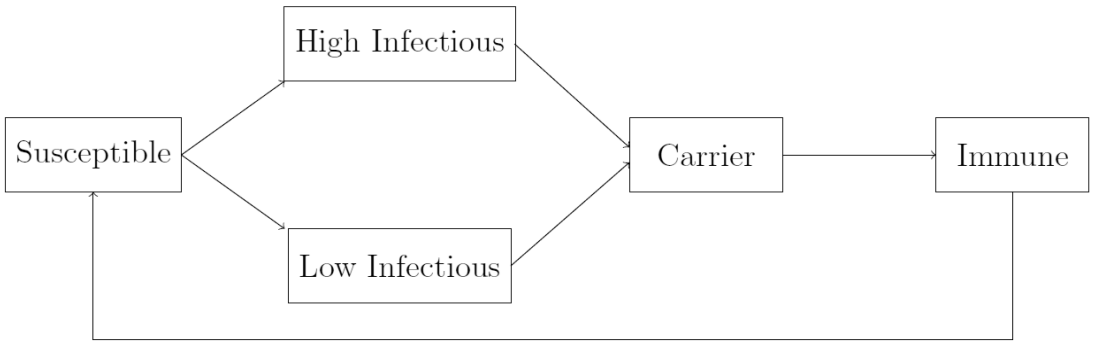

Figure 3.7: Representation of the model, where classes represented are S, susceptible; HI,high infectious; LI, low infectious; C, carriers; Im, immune. Reproduced from Fig 1 of Soumpasis and Butler [2009].

If the IE exceeds a critical value (IE_{cl}), the high propagation syndrome is triggered. If however the IE drops below the IE_{cl} the low propagation syndrome is triggered. After approximately 16 days ($\frac{1}{\gamma}$) pigs start to produce antibodies and stop shedding. This is assumed to be true for the high and low propagation syndrome. For a part of the period that pigs have circulating antibodies, they also carry the pathogen in internal organs without shedding (i.e. carrier pigs). Pigs are clear of *S.* Typhimurium in the internal organs after approximately 68 days ($\frac{1}{\Gamma}$), and have circulating antibodies for approximately 42 days ($\frac{1}{\kappa}$). After this period, antibody levels drop below a limit and the pigs again become susceptible (S) to infection.

3.4.2 Deterministic model

For the deterministic model, β, ϵ and IE_{cl} could not be found in published literature or experimental data. As such a scenario analysis was run that simulated a previous lon-

gitudinal study , in which three different compartments (a 'negative', 'intermittent' and 'positive') of a subclinical infected herd were followed bacteriologically and serologically. The farm was selected with criteria that made it as representative as possible of farming procedures. This model was validated using information from the previous study. The median parameters $\beta(0.165)$, $\epsilon(0.70)$ and $IE_{cl}(0.12)$ were used in construction and application of the stochastic model.

3.4.3 Stochastic model

The model uses the "τ leap method" as described by Keeling and Rohani [2008], using a time step of 1 day, with the following possible events: pigs move from the susceptible to the high infectious or low infectious class, recovery of the high infectious class, recovery of the low infectious class, recovery of the carrier class and loss of immunity (move from immune to susceptible). At each time step, which event happens and calculations of the number of events is based on a Poisson distribution, as shown in Table 3.1. At the end of each time step, the population for each class is updated and introduced as a starting value for the next time step.

Table 3.1: Events and number of events per time step using the "τ- leap method." Reproduced from Table II of Soumpasis and Butler [2009].

Name	Number of events	Event
High infection	$M1$ =Poisson$(\tau \times [\beta \times S \times (HI + \epsilon \times LI)/N])$	$S \mapsto S - M1, HI \mapsto HI + M1$
Low infection	$M2$ =Poisson$(\tau \times [\beta \times S \times (HI + \epsilon \times LI)/N])$	$S \mapsto S - M2, LI \mapsto LI + M2$
Recovery of HI pigs	$M3$ =Poisson$(\tau \times [\gamma \times HI])$	$HI \mapsto HI - M3, C \mapsto C + M3$
Recovery of LI pigs	$M4$ =Poisson$(\tau \times [\gamma \times LI])$	$LI \mapsto LI - M4, C \mapsto C + M4$
Recovery of carrier	$M5$ =Poisson$(\tau \times [\Gamma \times C])$	$C \mapsto C - M5, Im \mapsto Im + M5$
Loss of immunity	$M6$ =Poisson$(\tau \times [\kappa \times Im])$	$Im \mapsto Im - M6, S \mapsto S + M6$

The IE governs the probability of the movement of pigs to either of the two infectious classes, HI and LI. For the stochastic model, a decision has to be made for which event will happen, HI or LI, depending on the IE. To do this, an IF/ELSE condition statement

was applied between the two types of infection, triggering in this way for either syndrome.

3.4.3.1 Starting values

A scenario analysis was run to explore the relationships of the probability of disease extinctions and the prevalence of each class and risk group at the end of the fattening period with the total population size of the compartment (TPC or N) and the starting conditions of infection (SCI), which represent the IE at the beginning of the fattening period.

TPC should have more than 200 pigs but less than 400 pigs for welfare and management reasons. For realistic farming conditions and populations, the starting conditions for the scenario analysis regarding TPC was an array from 200 to 400, increasing by 5 pigs for each simulation. Only HI pigs were introduced into the model, given they have "absolute" transmitability and their population directly reflects the IE, whereas the population of LI is related to IE using the reduced transmitability factor ϵ. The IE could be however, any combination of HI and LI pigs. The simulations for each compartmental population starts with 1 HI pig and was increased by 1 up to 10 HI pigs, and thereafter was increased by 5 until the percentage of the population of HI pigs reached 100%.

Each simulation regarding the SCI was run for 5,000 replicates, and the occurrence of disease extinctions and the prevalence of each class of pigs at the last day of monitoring were recorded. Disease extinction is defined as "cases where HI and LI pigs are absent from the compartment so the infection cannot propagate anymore." The probability of extinctions and the mean and standard deviation of the prevalence for each class of pigs (also "risk groups" of cecal-, culture- and sero-positive pigs) were calculated and stored

for each simulation, together with the TPC and SCI. Cecal-positive pigs were considered to be pigs in the HI and LI classes, carry the pathogen in the intestinal contents, culture-positive pigs in HI/LI and C classes carry the pathogen in the internal organs including intestinal content, and seropositive pigs in the C and Im classes, which carry antibodies against the pathogen. The first two risk groups pose a risk of introducing the pathogen into the slaughterhouse while the third is used at the herd level (i.e. ZAP).

The model was run for 113 days, starting with pigs that were 61 days old, as this was calculated to be the mean age that pigs lose maternal immunity. The last day of the model (day 174) is thought to be the average day pigs leave the farm to go to slaughter. The stochastic model was validated in relation to the deterministic model, using the predicted mean prevalence of the different classes/risk groups for the range of TPC and SCI. The mean prevalence of the stochastic model approximated the prevalence predicted by the deterministic model, at least for the TPC and SCI where the probability of extinctions were approximately zero.

The model and analysis were written in Python programming language v.2.5.1, using the scientific libraries Scipy/Numpy for numerical calculations. Statistical interpretation of the data were done using R.

3.4.4 Model output

It was found that the total population size of the compartment (TPC) had a considerable effect on the probability of extinction, notably with high levels of starting conditions of infection (SCI). It can be seen from Figure 3.8, that an increase in the starting conditions

of infection resulted in an increase in the probability of extinction. This is likely to be due to a large immune period (approximately 42 days), since the majority of animals would have gone through the different infection stages and remain within the immune class, at the point of slaughter. It was also shown that as the total size of the compartment increased, the probability of extinction decreased.

Figure 3.8: Scatterplot of the probability of extinction over the starting conditions of infection for various compartment sizes. Reproduced from Fig 2 of Soumpasis and Butler [2009].

3.4.5 Critique

The differentiation of the infectious states are well justified. A novel approach is applied in order to decide which disease syndrome is triggered, however a lack of data is available in order to fully validate the number of highly infectious pigs within a unit. Disease

extinction is defined to be when high infectious and low infectious pigs are eradicated. However, this fails to account for any carriers within the model, which would be counted as 'infected.'

3.5 Discussion

Clearly there are quite diverse models describing *Salmonella* transmission around a pig herd. As such, there is a need for further evidence that describes *Salmonella* dynamics within a pig unit and enables the industry to make a more informed decision with regard to *Salmonella* control. As management practices and farm structure between farms vary considerably, the need to develop models describing varying structures and practices to those developed previously is warranted.

All of the models developed here, with the exception of Hill et al. [2007], use an all-in-all-out methodology, which is the general methodology used on farm; this is also evident within Chapter 2. All models described within this chapter adopt the discrete time modelling approach, which is arguably unrealistic for such a system, as events unfold continuously, which suggests a continuous time framework is more realistic.

The *Salmonella* states used by Hill et al. [2007] are the more conventional states (SICR) that are used within mathematical models. Ivanek et al. [2004] incorporates a latent period into the model, and although a latent period could be included, as its duration is small, it is thought to have little impact on the dynamics. The use of a two-directional transition between infectious and carrying animals (i.e. infectious $\Leftrightarrow$ carrying) by Ivanek et al. [2004] and Lurette et al. [2008] however is profound. Findings in the literature have

identified a possibility for intermittent shedding (Kranker et al. [2003], Osterberg and Wallgren [2008]) and an increased possibility of re-shedding the bacteria when levels of stress are increased (Lo Fo Wong et al. [2002], Callaway et al. [2006]). Consequently, this is thought to be an important inclusion within a model of *Salmonella* spread.

The inclusion of different infectious categories by Soumpasis and Butler [2009] is very well justified, as a number of studies have shown a large distribution of shedding between animals, for example Gray et al. [1995], Scherer et al. [2008]. Although this is a possibility, a lack of data in order to justify and validate the model in terms of numbers of animals within each category, inhibits the inclusion of these additional categories.

Chapter 4

Literature review used in estimation of parameters

This chapter describes the parameter values used within the models, where an informed estimate could be made. A full literature review was carried out in order to determine parameter estimates. Although some parameters were not quantifiable, plausible estimates were used wherever possible.

4.1 Herd structure

The structure of the herd used within the model is of a finishing unit[1] taken from BPEX [2006], in which it states the number of pigs per pen (N) on a 1000 place, fully slatted finisher house (as used here; see Figure 4.1) is $N = 25$. The unit has 40 pens in total, where there are 20 pens on each side of a corridor ($PensPerSide = 20$). Furthermore, according to BPEX and MLC [2007], pigs spend an average time of 108 days in the feeding herd, thus $T_{max} = 108$ days.

As this style of unit is fully slatted, it shall be assumed that the majority of faeces

[1] Although farms can use the structure as described here, it is important to note that this style of farming is not exclusive, and some pig farms will have differing structures and practices.

shed by the animals would fall into the slurry pit rather than stay within the room. As such, the proportion of faeces that remains in a room (*prop*) has been set to $prop = 0.4$; however, this value will be variable.

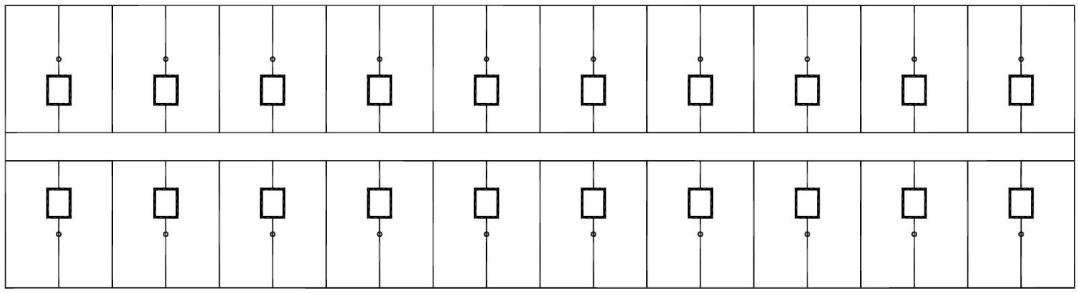

Figure 4.1: Structure of a 1000 place, fully slatted finisher house as in BPEX [2006]. A corridor separates the 40 pens into two rows with feeding troughs between the neighbouring pens (small rectangular box). A slurry pit is found beneath the pens which is emptied at certain periods.

A model of a solid floored finishing unit has also been developed, again adapted from BPEX [2006], in which a 560 place straw-based wean to finish building is described, as shown in Figure 4.2. Although the number of pens within the buildings are different, identical values will be used to ensure a direct comparison of the models can be made.

4.2 Individual pig epidemiological parameters

Pigs that recover from infection become temporarily immune (i.e. they cannot be infected for a certain period of time, of mean $\frac{1}{\nu}$), which is an assumption also adopted by Hill et al. [2007] (who use a fixed length of 10 days) and Soumpasis and Butler [2009]. However, Ivanek et al. [2004] allow pigs to become susceptible immediately after the carrier stage of infection. As little is known about the length of immunity, it is assumed that the actual duration is unknown, and a value of approximately 2 days will be used; therefore, $\nu = 0.5$ day^{-1}.

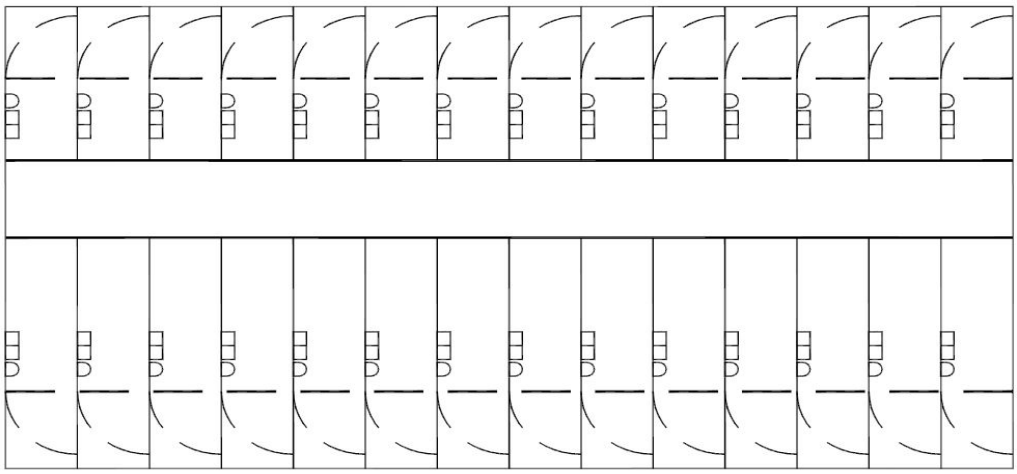

Figure 4.2: Structure of a 560 place, straw-based wean to finish unit as in BPEX [2006]. A solid wall divides the 2 rows of pens and a scraping passage runs along either side of the building.

In order to estimate transition rates regarding infection and immunity, various studies were reviewed.

➤ **Wood et al. [1989]**

A study by Wood et al. [1989] orally inoculated pigs with *Salmonella* Typhimurium with an average dose of 1.43×10^{10} cfu. Pigs were exposed at 7 to 8 weeks old and kept on concrete floors in isolation rooms housing ≤ 12 pigs. The study was conducted in a series of 3 experiments of 1, 6 and 28 weeks duration. Within each experiment, tonsillar and rectal swab specimens, blood culture, serum and faecal samples were taken at various time points during the study.

Experiment 1. Eight 6 week old barrows were allotted at random to 2 isolated groups of 4 pigs. One group (principals) were exposed and the other were unexposed controls. After exposure, samples were taken daily until necropsy. Two infected pigs were necropsied

at random on postexposure (PE) day 2, and 2 controls on PE day 3. The remaining infected pigs were necropsied on PE day 4 and 7, with the 2 remaining controls on PE day 8.

Experiment 2. Fourteen 5 week old pigs (11 barrows, 3 gilts) were allotted at random to 2 isolated groups of 10 principals and 4 controls. After exposure, faecal samples were collected on PE days 2, 6 and 7, and weeks 2-6. Four principals died (PE day 6 (2 pigs) and 7 (2 pigs)) and were not used for necropsy. The remaining 6 were necropsied at random 2, 4 and 6 weeks PE (2 each time). Controls were necropsied at random at 2 (2 pigs), 4 (1 pig) and 5 (1 pig) weeks after exposure.

Experiment 3. Twenty three pigs (13 barrows, 10 gilts) were reared in isolation from 2 days to 6 weeks old. All pigs were exposed. Faecal samples were collected on PE days 2 and 7, and weekly thereafter at 2 to 28 weeks. Two pigs died week 2 after exposure and were not used in the study. The remaining 21 were necropsied at random at 4 (2), 8 (3), 12 (3), 16 (3), 20 (3), 24 (4) and 28 (3) weeks PE.

Results. The main results of the study (obtained from Experiment 3) found *S.* Typhimurium in all faecal samples, 99.4% of tonsillar swab specimens and 96.4% of rectal swab specimens during the first 6 days post exposure (PE). Between 83% and 100% of faecal samples were positive through PE week 22, which then decreased to 29% at week 23 and 14% at week 24 (see Figure 4.3). At least 60% of tonsillar swab specimens and 50% of rectal swab specimens were positive up to PE week 20, after which the levels declined.

➤ **Gray et al. [1995]**

A study by Gray et al. [1995] inoculated groups of pigs at 7 weeks of age (day 0) with

Figure 4.3: Recovery of *S.* Typhimurium from faecal samples, tonsillar and rectal swabs taken from pigs. Reproduced from Fig 3 of Wood et al. [1989].

S. Choleraesuis. Prior to this, pigs were randomly divided into 3 groups and housed in separate isolation facilities. Group 1 ($n = 15$) were challenged intranasally with 1 ml of strain 3246pp at $1x10^8$ cfu/ml. Group 2 ($n = 16$) were challenged via gastric route using gelatin capsules again with 1 ml of strain 3246pp at $1x10^8$ cfu/ml, and group 3 ($n = 4$) served as uninoculated controls. At various points throughout the study, tonsil, nasal and rectal swabs were taken, as well as culture of faecal samples were taken. Faecal pools were also taken which consisted of fresh 1 - 2 g samples of faeces randomly collected from 10 different areas in a pen. Four pigs from group 1 and 2 and one group 3 were euthanised and necropsied at 2, 4, 6 and 12 weeks post-inoculation (PI) - only 3 group 1 pigs were necropsied at 12 weeks. At necropsy, various tissues were collected including the tonsil, lymph nodes, ileocolic junction and colon.

Results. *S.* Choleraesuis was recovered from 8 of 15 faecal pools (day 1/2/3, week

1/4/8/9/11) from group 1 versus 9 of 15 (day 1/2/3, week 4/6/7/8/10/11) from group 2. Group 1 had a markedly higher magnitude of shedding (see Figure 4.4), but both groups shed low levels sporadically after 2 weeks post-inoculation (PI). It is important to note here that Figure 4.4 appears to be inconsistent with the paper's stated results, as the figure shows the presence of *Salmonella* at week 2 from group 1.

Figure 4.4: Quantitative recovery of *S.* Choleraesuis from faecal pools. Reproduced from Fig 1 of Gray et al. [1995].

The percentage of positive samples was higher for intranasally challenged pigs until week 12, when gastric challenged pigs had the same proportion positive (11%). Results indicate that regardless of route of infection, *S.* Choleraesuis can persist in the tonsil, ileocolic lymph node, ileocolic junction and colon and can be excreted in faeces for at least 12 weeks. Therefore, upon infection with 10^8 organisms and after resolution of

initial clinical signs, the bacteria persist at relatively low levels in clinically normal pigs establishing a carrier state; where a carrier state is defined here as a pig that is infected with the bacteria in some form, whether asymptomatic or not. In a study by Smith and Jones [1967], 10^6 cfu of *S.* Choleraesuis/g faeces was shed by pigs during acute infection following challenge with 10^{10} cfu, whereas in this study, a challenge of 10^8 cfu saw clinical illness and a magnitude of shedding of 10^3 cfu/g, which indicates carrier animals shed low levels of *S.* Choleraesuis in faeces.

➤ **Kranker et al. [2003]**

Kranker et al. [2003] selected 3 Danish farrow-to-finish pig herds with moderate to high levels of *S.* Typhimurium infection for the study. Two farms (650 and 440 sows) were two-site operations, with the remaining farm a three-site, 300 sow operation; all of which were self supplying. In each herd, 10 litters were randomly selected and in each litter the ears of 6 randomly selected piglets were tagged. Litters from each herd were divided into two groups of 5 litters. Therefore, on each farm, there were two cohorts consisting of 30 pigs each, yielding a total of 180 piglets at the start of the study.

Blood and faecal samples were collected: (i) prior to weaning (faeces only); (ii) mid-way through the nursery period; (iii) just before leaving the nursery; (iv) monthly in the finishing unit and (v) just prior to slaughter.

Results. On each farm, *Salmonella* was primarily found in the nursery and finisher units and it was only occasionally found in gilts and sows. In all 3 herds, only *S.* Typhimurium was isolated during the entire study period. Shedding reached a peak in the nursery (9 weeks of age) and declined during the finishing period (see Figure 4.5). The

serological response was observed approximately 30 days later and on average, reached its peak in the mid finishing period (17 weeks of age).

Figure 4.5: Average prevalence of *Salmonella* in blood and faecal samples. Reproduced from Fig 1 of Kranker et al. [2003].

A total of 88 pigs were found to be shedding *Salmonella* on more than one occasion. To estimate the shedding time, it was assumed that shedding either began at least $3\frac{1}{2}$ days prior to the first isolation and lasted at least 3 days after the last isolation, or began 1 week prior to the first isolation and lasted 1 week after the last isolation. An individual pig was considered at risk (i) for as long as it was culture negative or (ii) if it was culture negative on two or more successive occasions. The overall mean shedding time was therefore estimated to be 18 or 26 days depending on the assumptions.

➤ **Osterberg and Wallgren [2008]**

Osterberg and Wallgren [2008] inoculated groups of pigs with 3 different doses of 2 different strains of *Salmonella*. Pigs were monitored for 8 weeks with respect to *Salmonella* excretion and the presence of antibodies to salmonellae in serum. Six groups of 6 pigs were

used and split accordingly. Pigs were inoculated orally on day 0 with 0.65×10^3, 0.65×10^6 and 0.65×10^9 cfu of *S.* Typhimurium in groups T3, T6 and T9 respectively. The other groups, Y3, Y6 and Y9 were inoculated in the same way with *S.* Yoruba. Individual faecal samples were collected before the pigs were infected, and after infection samples were collected daily during the first week, 3 times a week for the next 3 weeks and twice thereafter.

Results. In general, it was found that pigs shed *Salmonella* species continuously for 4 weeks and intermittently during the next 4 weeks. Both serotypes were isolated from the faeces of 5/6 of the pigs challenged with 0.64×10^6 cfu on the first day after infection. Pigs infected with 0.65×10^6 cfu *S.* Typhimurium shed the bacteria for up to 28 days, whereas those infected with 0.65×10^9 cfu shed for up to 56 days (see Figure 4.6).

All the pigs in group T9 seroconverted to *S.* Typhimurium within 2 weeks after infection, and the titres of serum antibodies remained at a high level for the duration of the study. In group T6, 5/6 seroconverted to *S.* Typhimurium but at lower titres, which decreased from day 35 onwards.

➤ **Gray et al. [1996a]**

A study by Gray et al. [1996a] divided 40 pigs into 3 groups; group 1 ($n = 12$) were challenged at 7 weeks of age with 10^8 cfu of *S.* Choleraesuis by intranasal inoculation. One day postinoculation (p.i.), group 2 naive pigs ($n = 24$) were commingled with group 1 pigs, and group 3 ($n = 4$) served as uninoculated controls. All pigs were culture negative for *Salmonella* species prior to challenge. Throughout the study faecal samples, as well as tonsil, nasal and rectal swabs were taken from each individual pig. At necropsy, tissue samples (tonsil, lymph nodes, colon among others) were taken.

Figure 4.6: Days on which individual pigs shed *Salmonella* in their faeces after being inoculated with different doses of *Salmonella*. Reproduced from Table 1 of Osterberg and Wallgren [2008].

Results. After challenge, all pigs in group 1 were shedding *S.* Choleraesuis on day 1 p.i. At least 16% of group 2 pigs were shedding *S.* Choleraesuis by day 2 p.i. which increased to 88% by day 11. From Table 4.1, shedding in group 1 peaked on day 8 p.i. while group 2 peaked on day 9 p.i. The challenged pigs (group 1) shed the bacteria for 34 days and again after 7 weeks. The naturally exposed pigs (group 2) however, only shed the bacteria for 26 days and again after 8 weeks. Tissue samples (including Tonsil, ICJ, ICLN and colon) from the naturally exposed pigs (group 2) were positive up to 12 weeks, compared to 9 weeks for the challenged pigs (group 1).

Table 4.1: Magnitude of faecal shedding. Reproduced from Table 1 of Gray et al. [1996a].

Time of sampling	$\log_{10}$ cfu/g		
	Group 1	Group 2	Environment
Day 1	2.61	NA[a]	2.61
Day 2	1.55	+[b]	2.55
Day 3	2.55	+	1.86
Day 4	ND[c]	0.64	2.29
Day 5	3.26	+	2.98
Day 6	3.35	0.46	1.60
Day 8	3.65	0.83	2.03
Day 9	2.97	1.51	2.25
Day 11	2.70	0.31	1.62
Day 13	1.73	0.43	1.00
Day 16	2.08	1.11	1.81
Day 19	1.72	0.49	1.35
Day 23	2.45	−[d]	1.08
Day 26	1.11	0.59	1.11
Day 30	2.25	−	2.10
Day 34	1.77	−	0.55
Week 6	−	−	−
Week 7	0.75	−	1.11
Week 8	−	0.63	−
Week 9	−	−	−

[a] NA, not applicable.
[b] +, positive.
[c] ND, not done.
[d] −, negative.

❒ Literature summary and parameter justification

Clearly all the studies discussed here are somewhat contradictory and thus compromises must be made in order to try and obtain reliable estimates of parameters. As *S.* Typhimurium is the most predominant serotype, studies also focusing on this serotype will be chosen. Although Wood et al. [1989] orally inoculated pigs with *S.* Typhimurium, which is the serotype of interest, the duration of shedding was found to be particularly long, and does not concur with any other study. Furthermore, the inoculation dose could potentially be much higher than natural exposure and is thus not realistic. Also, as it is the oldest study, more modern methods are thought to be more accurate and reliable. Although the

study by Gray et al. [1995] also gives a long shedding time, it is for a high artificial dosage of a different serotype, and will therefore not be used.

In order to estimate the mean duration of infectiousness $\left(\frac{1}{\gamma}\right)$, a combination of the studies by Osterberg and Wallgren [2008] and Kranker et al. [2003] shall be used. Both studies use *S.* Typhimurium and find the mean shedding time to be 28 or 18-26 days respectively. Hence the time pigs remain infectious shall be taken as having rate parameter $\gamma = \frac{1}{26}$ day^{-1}. Although Gray et al. [1996a] use *S.* Choleraesuis, the duration of shedding is similar to Osterberg and Wallgren [2008] and Kranker et al. [2003]. What makes this study of particular importance is the use of natural infection. Very few studies have looked directly into *Salmonella* carriage in pigs.

Figure 4.5 as shown previously, from the study by Kranker et al. [2003], shows seroprevalence to rise for approximately 60 days and then start to decrease. Although it does not decrease to low levels, the drop in seroprevalence may indicate that *Salmonella* carriage has finished; however this assumption ignores the possibility of asymptomatic carriers. Assuming the increase in seropositivity is linked to *Salmonella* carriage, the mean duration of carriage $\frac{1}{\epsilon}$ shall be 60 days.

An important point to note is the use and definition of the term 'carrier' pig. A common definition, as in Gray et al. [1995], is that a carrier pig is a pig that carries the bacteria within its system and can excrete the bacteria in its faeces, and is thus infectious. The way in which a carrier pig shall be defined here is a pig that only carries the bacteria internally but without excreting the bacteria in its faeces, and therefore does

not contribute to infection; this is similar to the usage of Hill et al. [2007]. It is supposed that carrier pigs can revert to a fully infected state (i.e. infected and excreting bacteria). The rate at which this occurs is likely to be very small as pigs will only start re-excreting with any stress imposed. It is thought that this rate is likely to be small within the farm, and increase rapidly when transported to the abattoir. As such, the rate at which a carrier pig becomes re-infectious is taken to be $\delta = 1/108$ day^{-1} (i.e. $1/t_{max}$) as although unlikely to happen, there is still a possibility of occurrence.

4.3 Bacterial survival

Pigs that are infected and are shedding the bacteria, could shed up to 10^7 cfu *S.* Typhimurium per gram of faeces (Gutzmann et al. [1976]). The average faecal dry matter output is approximately 225 g per day (Leek et al. [2005]; discussed further in Section 4.4). A study by Jensen and Baggesen [2005] found the majority of pigs (83%) to shed less than 100 cfu per gram faeces. Assuming this is an average concentration of *Salmonella*, the rate of *Salmonella* shedding (λ) is approximately 2.25×10^4 cfu day^{-1}.

Any bacteria shed into the environment will clearly survive for a limited period of time. A study by Nicholson et al. [2005] finds that the maximum *S.* Typhimurium survival period in unturned/turned (composted) pig farm yard manure is either 4 or 16 days respectively, and either 16 or 32 days within pig slurry following land spreading. A report by EFSA [2010] has a *Salmonella* decay rate of (θ) with a value of 0.04 day^{-1}, which is obtained from a study by Gray and Fedorka-Cray [2001]. This study found *S.* Choleraesuis to survive for at least 3 months in wet swine faeces and 13 months in dry faeces. Furthermore, a study by Jensen et al. [2006] found *S.* Typhimurium to survive for the entire test period

(7 weeks) within outdoor shelter huts. The difficulty with estimating *Salmonella* survival time however, is the fact that the estimate depends on the numbers of bacteria within the environment initially. Consequentially, the true *Salmonella* survival time is unknown. Assuming a month is 28 days, the study by Gray and Fedorka-Cray [2001] shall be used, which found *Salmonella* to survive in faeces for at least 3 months; thus an average survival time of 84 days shall be assumed, which in terms of the death rate of bacteria (l) is $l = \frac{1}{84}$ day^{-1}.

4.4 Between pig transmission

4.4.1 Transmission via faecal consumption

Any faeces that are shed into the room are available for consumption. EFSA [2010] took the mean mass of faeces ingested by a finisher pig to be between 0 and 100 g per day, with a concentration of between 0 and 10^7 cfu/g *Salmonella* in contaminated faeces. Within the models presented, the transition associated with consumption of a single bacterial cfu (in its simplest form) is $p\kappa SW$ per day, where p is the probability of infection from bacterial consumption, κ is the proportion of cfu ingested, S is the number of susceptible animals and W is the amount of bacteria in the environment. As such, κ should be the proportion of cfu present ingested by 1 pig in 1 day, i.e. $\frac{\text{amount of faeces ingested}}{\text{total faeces available}}$. This is clearly highly dependent on the values obtained from EFSA [2010] in terms of faecal availability. The total amount of faeces available however will be dependent on farm structure, which should scale with the number of pigs present and the proportion of faeces that remains available. Therefore, the amount of faeces available would be ($N \times PensPerSide \times 2 \times prop \times f \times$ faeces shed per pig per day); where f is the approximate average number of days faeces that remain available. This is assumed to be 7 days for simplicity and to remain consistent

with weekly cleaning. As mentioned previously, Leek et al. [2005] find the average faecal dry matter output of approximately 225 g day^{-1}, however the amount of faeces this equates to is unknown. Furthermore, it is shown that age and diet have a big effect on the amount of faeces shed. Assuming pigs ingest an average of 50g faecal dry matter per day, the value of κ, depending on herd structure is:

$$\kappa_{SingleSlatted} = \frac{50}{25*20*2*0.3*7*225} = 1.06 \times 10^{-4}.$$

$$\kappa_{MultipleSlatted} = \frac{50}{25*5*2*0.3*7*225} = 4.23 \times 10^{-4}.$$

$$\kappa_{Solid} = \frac{50}{25*20*2*1*7*225} = 3.17 \times 10^{-5}.$$

When a pig ingests *Salmonella*, there is an associated probability of infection from this bacterial consumption (p). A study by Gray et al. [1996b] that infected groups of pigs with varying amounts of *S.* Choleraesuis (10^9, 10^6 and 10^3) found that short term persistence can occur with a dose of 10^6 cfu. A study by Osterberg et al. [2009] found that in general, the dose had a greater impact on response rather than serovar; therefore assuming that *S.* Choleraesuis is representative of *Salmonella* spp. in general, then it can be assumed that 10^6 cfu is a typical infectious dose. A dose of at least 10^6 cfu (*S.* Typhimurium) was required to cause detectable levels of *Salmonella* in the faeces in a study by Osterberg and Wallgren [2008], which verifies the value. As p is the probability a pig is infected by 1 cfu, the probability of becoming infected by C cfu $= 1 - (1-p)^c$. Assuming approximately 90% of pigs become infected (in some form) after challenge with 10^6 cfu:

$$\begin{aligned} 0.90 &= 1 - (1-p)^{10^6} \\ \Rightarrow 1 - p &= 0.1^{10^{-6}} \\ \Rightarrow p &= 1 - 0.1^{10^{-6}} \\ &= 2.30 \times 10^{-6}. \end{aligned}$$

4.4.2 Other routes of transmission

Within the models there are certain parameters that are unquantifiable. The infection rate due to direct contact, β, and the cross infection rate between adjacent pens, α, are such parameters. Therefore, these values shall be variable, but have been generated in the first instance to produce results that appear to mimic reality. This will also be the case with the airborne infection parameter, ω.

4.5 Final parameter values

All parameters as described within the chapter are shown in Table 4.2.

Table 4.2: General model parameters and values

Parameter	Definition (units)	Parameter	Reference
N	Number of pigs per pen	25	BPEX [2006]
$PensPerSide$	Number of pens on either side of a corridor	20	BPEX [2006]
β	Infection rate	Unknown, assume 1.67×10^{-3}	None
γ	The rate at which a pig ceases to remain infectious (day^{-1})	$\frac{1}{26} = 0.03846$	Osterberg and Wallgren [2008], Kranker et al. [2003]
δ	The rate at which a carrier becomes re-infectious (day^{-1})	$\frac{1}{108} = 0.00926$	None
ϵ	The rate at which a pig ceases to carry the bacteria (day^{-1})	$\frac{1}{60} = 0.01667$	Kranker et al. [2003]
ν	Loss of immunity (day^{-1})	0.5	None
λ	Shedding rate (cfu day^{-1})	2.25×10^4	Jensen and Baggesen [2005], Leek et al. [2005]
κ	Proportion of cfu present ingested (day^{-1}): Single slatted	1.06×10^{-4}	EFSA [2010], Leek et al. [2005]
	Multiple slatted	4.23×10^{-4}	
	Solid	3.17×10^{-5}	
l	Bacteria death rate (day^{-1})	$\frac{1}{84} = 0.01190$	Gray and Fedorka-Cray [2001]
p	Probability of infection from bacterial consumption	2.30×10^{-6}	Gray et al. [1996b], Osterberg and Wallgren [2008]
α	Cross infection rate	Unknown, assume 1.14×10^{-6}	None
$prop$	Proportion of faeces that remains in a room	0.4	None
T_{max}	Time spent in unit (days)	108	BPEX and MLC [2007]
ω	Airborne infection rate	Unknown, assume 1.02×10^{-14}	None

Chapter 5

Modelling *Salmonella* spread within a slatted-floored unit

As the finishing stages are the last part of the pig's life cycle, it is likely that this part of the system poses a substantial risk to public health. As such, the models developed here focused on this stage of the production system. It is the growing/finishing stage that shows a high impact of *Salmonella* infection by stunting growth, which consequentially has economical implications. Also, any interventions to be implemented within the breeding unit are extremely expensive, and so are less likely to be economically viable. Furthermore, production units can have a high *Salmonella* prevalence in the breeding sector and a low *Salmonella* prevalence in the finishing sector (EFSA [2009]), and vice versa, which implies that interventions later on in the production line can be effective.

Clearly different farms have different farm practices and structures (see Chapter 2 for details of a BPEX study into farm practices) and so some generalisation must be implemented in the development of models of *Salmonella* spread. In this chapter, a model of *Salmonella* dynamics within a slatted-floored pig finishing unit, using a novel SICRS/W model, will be developed.

5.1 Modelling *Salmonella* spread within a single-roomed slatted unit

As previously mentioned, farm practice and management differs greatly between farms across the UK. This section shall consider a simple slatted-floored finishing unit, in the form of a single building, identical to that in Figure 4.1.

5.1.1 Model formulation

A susceptible - infected (infectious) - carrier - recovered - susceptible (SICRS) model incorporating environmental bacteria (W) was developed. The latent period was neglected due to its short time, which was thought to have little impact on the dynamics. The model incorporated transitions from carrier to infectious states as any stress imposed on a carrier pig could induce infectivity. Although the initial value of this parameter (δ) was small (see Chapter 4), extensions to the model (e.g. incorporating transportation) would affect its value. Although the use of four states regarding *Salmonella* infection (susceptible, infectious, carrier and recovered) results in a complex model, it is generally thought that all states exist and all have therefore been included for completeness.

Clearly some animals are susceptible to infection and there is a possibility that some animals will eventually recover. It is well known that some pigs do not shed the bacteria in their faeces, but are nevertheless infected with the bacteria. As such, the presence of 2 different states implies that there needs to be a differentiation between those animals that shed the bacteria and those that just carry the bacteria. Although other states could be used (as shown in Chapter 3) as data were not readily available to account for these extra categories, analysis of the model with these superfluous categories could be seen as futile.

In this model, there were 14 possible events (see Table 5.1). Fourteen parameters were used (as described in Chapter 4, Table 4.2), namely the number of pigs per pen N, the number of pens on either side of a corridor $PensPerSide$, the direct infection rate β, the airborne infection rate ω, the rate at which a pig ceases to be infectious γ, the rate at which a carrier becomes re-infectious δ, the rate at which a pig ceases to carry the bacteria ϵ, the loss of immunity rate ν, the bacterial consumption rate κ, the shedding rate λ, the bacteria death rate l, the cross infection rate α, the indirect infection probability p and the proportion of faeces that remains within the room *prop*. All parameters were assumed to be strictly positive. The total number of animals on farm ($2 \times N \times PensPerSide$) is denoted by P. A diagramatical representation of the model, which highlights the use of these parameters, can be seen in Figure 5.1.

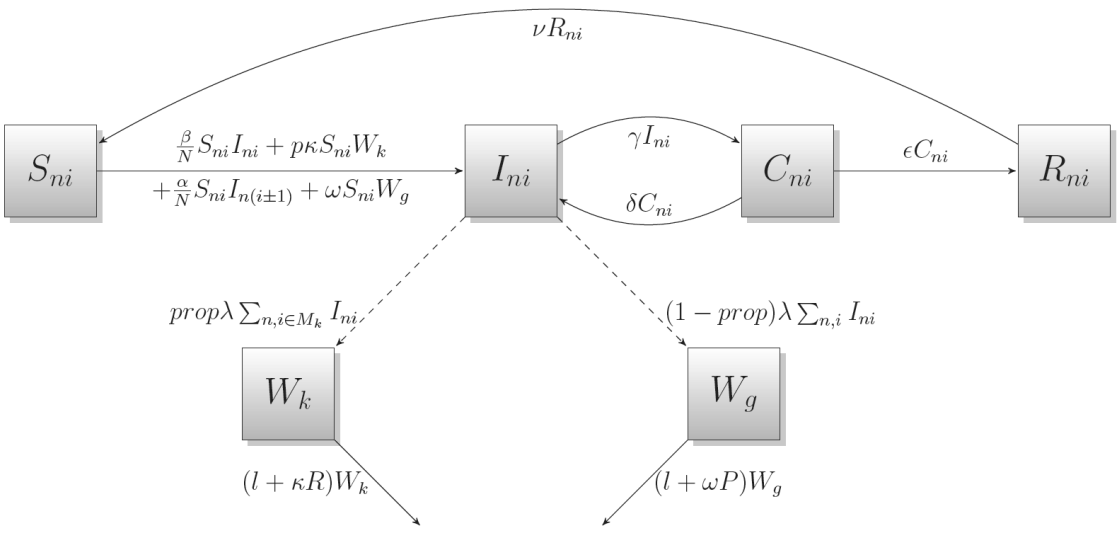

Figure 5.1: Flow diagram representing transmission routes and other processes described by Table 5.1 for pen i of row n, $n = 1, 2$, $i = 1, 2, \ldots, PensPerSide$. Note that this diagram is for the multiple-roomed model as described in Section 5.2. M_k is used to denote the set of pens within room k. As such, for the model described here, $k = 1$ and $M_1 = \{1, \ldots, 2 \times PensPerSide\}$.

Firstly, it is important to take account of the physical structure of the unit in order to fully explain the possible transitions within the model. The structure of the unit itself was identical to that in Figure 4.1 whereby there were 20 pens on either side of a corridor ($PensPerSide = 20$) with a fully slatted floor (BPEX [2006]). As the farm being modelled had fully slatted flooring, there was a corresponding proportion of faeces that remained available for consumption (*prop*). Feeding troughs were shared between neighbouring pens, resulting in the possibility of infection via direct contact between pigs in these pens, with rate parameter α. Airborne transmission is also a factor in the spread of *Salmonella* infection and a methodology similar to Noakes et al. [2006] was adopted when modelling airborne infection. Noakes et al. [2006] allow airborne transmission according to $\frac{pq}{VA}SI$, where $\frac{pq}{VA}$ is some form of airborne infection rate consisting of the ventilation rate (A), room volume (V), average pulmonary ventilation rate of susceptibles (p) and the quanta production rate per infector (q). Within the models presented here, rather than a dependency on infected pigs, the amount of bacteria within the general environment was considered of more importance regarding this route of infection, with an airborne infection rate parameter of ω.

In terms of pig movement, farms can operate on an all-in-all-out, batch or continuous flow system. Approximately half the industry operate on an all-in-all-out system, which was the methodology adopted here, and so the models should be representational of parts of the industry. Furthermore, the average number of pigs within a feeding herd has seen an increasing trend (up to an average number of 1,992 pigs in 2006), hence the number of animals within this system ($P = 1000$) is reasonable (BPEX and MLC [2007]). All pigs enter and leave the farm at the same time; i.e. pigs enter the model at $t = 0$ and

leave at $t = T_{max}$. It is however important to note that even within the all-in-all-out system, management practices can differ between farms. On some farms pigs are weaned and grown through to finishing in the same building (2 stage) and on others the pigs are weaned, grown and then moved to other buildings or sites for finishing (3 stage; Armstrong [2010]). The duration the model is run for accounts for the duration an animal would spend within the grower-finisher stages of production; this duration concurs with the findings from farms visited within the BPEX study (Chapter 2). The methodology that was adopted within the models was the 2 stage practice, as it was assumed stress was minimal and so as little movement as possible occurred. It was assumed that all pigs remain in the same pen until they leave; i.e. there was no mixing of pigs.

Denote the number of susceptible (S), infectious (I), carrying (C) and recovered (R) pigs in pen i of row n at time t as $X_{ni}(t)$, where $X = (S, I, C, R)$. Consider a closed population (in pen ni) of size N, which at time $t \geq 0$ consists of $S(t)$ susceptible, $I(t)$ infectious, $C(t)$ carrying and $R(t)$ recovered pigs. Infectious pigs are associated with a population of free-living bacteria within the local environment (W_d) and general environment (W_{gen}). It is important at this stage to recap the use of the term 'carrier' as defined in Chapter 4. Numerous publications have agreed that a 'carrier' state is present (Gray et al. [1995] and Morgan et al. [1987], for example), but the way in which the term is used within modelling differs. Here, it was assumed that a carrier pig is an animal that carries the bacteria internally (in the lymph nodes, for example); and is thus infected, but is not capable of passing on infection.

Within the model, when a pig became infectious, it was assumed it remains so for

a time that was exponentially distributed with mean γ^{-1}, and then became a carrier, which could either become re-infectious (at rate δ) or recover (at rate ϵ). Any recovered animals were temporarily immune for a time of mean ν^{-1} and could therefore not be re-infected, before returning to the susceptible class. During its infectious period, each infective host made contacts at the points of a homogeneous Poisson process of rate β; each such contact was with a pig chosen uniformly at random from those within the same pen; if the pig contacted was susceptible, it became infected. Similarly, infective hosts could contact pigs in neighbouring pens at rate α. During its infectious period, the host shed *Salmonella* into the environment at the points of a Poisson process of rate λ. Each host, whether susceptible, infectious, carrier or recovered, consumed bacteria from the local environment according to a Poisson process with rate $\kappa W_d(t)$; whenever a susceptible pig consumed *Salmonella*, with probability p the susceptible pig became infected. Finally, if not consumed, *Salmonella* survived in the environment for a time that was exponentially distributed with mean l^{-1}. This is referred to as an SICRS/W model.

More precisely, within a single pen set up, it was supposed the process $\{(S(t), I(t), C(t), W_d(t), W_{gen}(t)) : t \geq 0\}$ was a continuous time Markov chain on the state space $\{s, i, c \in \{0,1,2,...\}, 0 \leq s+i+c \leq N, w_d, w_{gen} \in \mathbb{Z}^+\}$. The multiple pen set up, as used within the model presented, has transition rates shown in Table 5.1. Furthermore, it was supposed that $R(t) = N - S(t) - I(t) - C(t)$.

In order to model the bacterial environment, the following methodology was applied. Let W_g denote the bacteria in the general environment (i.e. faeces that falls through the slats), W_d denote the bacteria within the local environment and *prop* be the proportion

Table 5.1: Transition rates used within the slatted single-roomed SICRS/W model

Event	State Transition	Rate
A susceptible becomes infectious by an infective within the same pen (ni)	$(S_{ni}, I_{ni}) \rightarrow (S_{ni}-1, I_{ni}+1)$	$\frac{\beta}{N} S_{ni} I_{ni}$
An infective in pen ni ceases to infect but remains carrying *Salmonella*	$(I_{ni}, C_{ni}) \rightarrow (I_{ni}-1, C_{ni}+1)$	γI_{ni}
A carrier in pen ni resumes shedding	$(I_{ni}, C_{ni}) \rightarrow (I_{ni}+1, C_{ni}-1)$	δC_{ni}
A carrier in pen ni recovers	$(C_{ni}, R_{ni}) \rightarrow (C_{ni}-1, R_{ni}+1)$	ϵC_{ni}
A recovered pig in pen ni becomes susceptible	$(S_{ni}, R_{ni}) \rightarrow (S_{ni}+1, R_{ni}-1)$	νR_{ni}
An infectious pig from a neighbouring pen ($n(i\pm 1)$) infects a susceptible in pen ni	$(S_{ni}, I_{ni}) \rightarrow (S_{ni}-1, I_{ni}+1)$	$\frac{\alpha}{N} S_{ni} I_{n(i\pm 1)}$
Indirect transmission from bacterial consumption	$(S_{ni}, I_{ni}, W_d) \rightarrow (S_{ni}-1, I_{ni}+1, W_d-1)$	$p\kappa S_{ni} W_d$
Indirect transmission via the airborne route	$(S_{ni}, I_{ni}, W_g) \rightarrow (S_{ni}-1, I_{ni}+1, W_g-1)$	$\omega S_{ni} W_g$
Bacteria shed into the general environment	$(W_g) \rightarrow (W_g+1)$	$(1-prop)\lambda \sum_{n,i} I_{ni}$
Death of bacteria within the general environment	$(W_g) \rightarrow (W_g-1)$	$l W_g$
Removal of bacteria from the general environment after airborne infection	$(W_g) \rightarrow (W_g-1)$	$\omega(\sum_{n,i}(I_{ni}+C_{ni}+R_{ni}))W_g$
Bacteria shed into the local environment	$(W_d) \rightarrow (W_d+1)$	$prop\lambda \sum_{n,i} I_{ni}$
Death of bacteria within the local environment	$(W_d) \rightarrow (W_d-1)$	$l W_d$
Consumption of bacteria by infectious, carrier and recovered pigs	$(W_d) \rightarrow (W_d-1)$	$\kappa(\sum_{n,i}(I_{ni}+C_{ni}+R_{ni}+(1-p)S_{ni}))W_d$

Note: Only state elements that are affected by the corresponding event are shown.
The full set of state elements is $\{(S_{ni}, I_{ni}, C_{ni}, R_{ni}) : n = 1, 2; i = 1, 2..., PensPerSide\}, (W_d, W_g)$.

of faeces that remains available for consumption. The amount of bacteria within the environment was time dependent, as the amount shed at any time depends on the number of infectious pigs. Furthermore, as the infectious stages process $(W_d(t), W_g(t))$ experiences transmissions at a faster rate than the infection process $(I(t))$, allowing infectives and bacteria to increase/decrease by 1 during simulation (as suggested within Table 5.1) was not ideal. As such, it was assumed that W_g and W_d evolve deterministically between transitions of (S, I, C) according to:

$$\frac{dW_g}{dt} = (1 - prop)\lambda I - (\omega P + l)W_g, \tag{5.1}$$

$$\frac{dW_d}{dt} = (prop)\lambda I - (\kappa P + l)W_d. \tag{5.2}$$

The local environment equation can be solved as follows:

$$\frac{dW_d}{dt} + (\kappa P + l)W_d = (prop)\lambda I.$$

Using an integrating factor of $e^{(\kappa P+l)t}$, then

$$\begin{aligned} e^{(\kappa P+l)t}\frac{dW_d}{dt} + (\kappa P + l)e^{(\kappa P+l)t}W_d &= (prop)\lambda I e^{(\kappa P+l)t} \\ \Rightarrow \frac{d}{dt}(e^{(\kappa P+l)t}W_d) &= (prop)\lambda I e^{(\kappa P+l)t} \\ \Rightarrow e^{(\kappa P+l)t}W_d &= \int (prop)\lambda I e^{(\kappa P+l)t} dt \\ &= \frac{(prop)\lambda I}{\kappa P + l} e^{(\kappa P+l)t} + A \\ \Rightarrow W_d &= \frac{(prop)\lambda I}{\kappa P + l} + Ae^{-(\kappa P+l)t} \end{aligned}$$

for some constant A. Suppose now (S, I, C) makes a transition at time T, and that $(I(T), W_d(T)) = (i, w)$. Then

$$A = w - \frac{(prop)\lambda i}{\kappa P + l}.$$

Also let τ be the time until the next transition of (S, I, C) then:

$$W_d(T+t) = we^{-(\kappa P+l)t} + \frac{(prop)\lambda i}{\kappa P + l}(1 - e^{-(\kappa P+l)t}),\ 0 \leq t < \tau. \tag{5.3}$$

The evolution of the general environment can be calculated in the same manner as above. This results in:

$$W_g(T+t) = we^{-(\omega P+l)t} + \frac{(1-prop)\lambda i}{\omega P + l}(1 - e^{-(\omega P+l)t}),\ 0 \leq t < \tau. \tag{5.4}$$

In order to simulate the time to the next event, Poisson thinning was used, which is described in detail by Ross [2007]. In order to simulate a nonhomogeneous Poisson process, a simulation of a Poisson process and then randomly thinning its events can generate the desired nonhomogeneous Poisson process. There are various methods that can be used to simulate such a process, such as rejection sampling and the thinning method. The thinning algorithm is the most efficient however, as it has the fewest number of rejected event times. An algorithm for generating a nonhomogeneous Poisson process is given in detail by Ross [2007]. In order to implement Poisson thinning for this model, the following algorithm was used.

Let X_t denote the state at time t, and q_{ij} be the transition rate of moving from state i to state j. The sum of the frequencies of all possible events from Table 5.1 is generated and denoted by $TotalRate$. The upper bound of this rate is also generated and denoted by $UpperTotalRate$. The algorithm is then:

Step 1 : Set $t = 0$.
Step 2 : Generate an inter event time, T from the exponential distribution with mean $\frac{1}{UpperTotalRate}$.
Step 3 : $t = t + T$. If $t > T_{max}$ stop.
Step 4 : Generate a random number U, uniformly distributed on $[0, 1]$ and accept event time t if $U < \frac{TotalRate}{UpperTotalRate}$, where $TotalRate$ is evaluated at the proposed event time t. Else go to step 2.
Step 5 : Generate a random number V, uniformly distributed on $[0, 1]$.
Step 6 : When k is the smallest value such that $\sum_{\substack{1 \leq j \leq k, \\ j \neq i}} q_{ij} \geq V\ TotalRate$, set $X_t = k$. Go to step 2.

The model began at the start of the grower/finisher stage of production, as such, within an infected herd, there is a prevalence associated with weaners entering the unit. A report by AHVLA [2011], showed that individual animal prevalence varies greatly, but is on average approximately 17% in weaners and growers; for simplicity, it was therefore assumed that 20% of pigs that enter the unit were infected in some manner. However, within the report, the state of the animal is not stated. Although it would be unlikely that all animals would be shedding the bacteria, it is thought that the majority would be in the early stages of infection. As such, within the unit, a random 15% of pigs were classified as Infectious, and a further 5% considered to be Carriers. Parameter values used were those found in Table 4.2.

In order to reduce the complexity of the model, a number of assumptions were made. It was assumed that the unit operated on an all-in-all-out basis, which is the general methodology used on farm. It was also assumed that no mortality or removals of pigs occur

prior to slaughter, i.e. constant number of pigs. Although this is not necessarily true, it is an assumption that is often used in models in order to be able to understand the dynamics. Furthermore, pigs were assumed to be the only source of infection.

All numerical work was carried out in MATLAB® 7.10 running under Microsoft® Windows® on a desktop personal computer.

5.1.2 Model output

A simulation of the model was run for 15,000 simulations in order to obtain an average prevalence on an infected farm at the end of the finishing stage, prior to slaughter. The model found an average prevalence of $\approx 15\%$ (150 pigs), where prevalence includes the number of infectious and carrying pigs, with $\approx 5.5\%$ (55 pigs) of these classed as infected and excreting, as shown in Figure 5.2. Clearly the majority of pigs were susceptible at the end of the finishing stage, whereas a small number of pigs were recovered. As the infectious and carrier classes were of most interest, both within the baseline model and when analysing interventions, the susceptible and recovered class shall not be analysed in great detail.

A plot of a trajectory from the model (Figure 5.3) showed a consistently higher number of carrying pigs compared to infectious pigs, with both states potentially starting to level off towards the end of the finishing period.

5.1.2.1 Model 'validation'

Validation of mathematical models is extremely complicated. The definition of 'validate' is to "examine (data etc) for incorrectness or bias; confirm or test the suitability" (Brown [2002]). It is therefore incredibly complicated to fully validate a model as by the nature

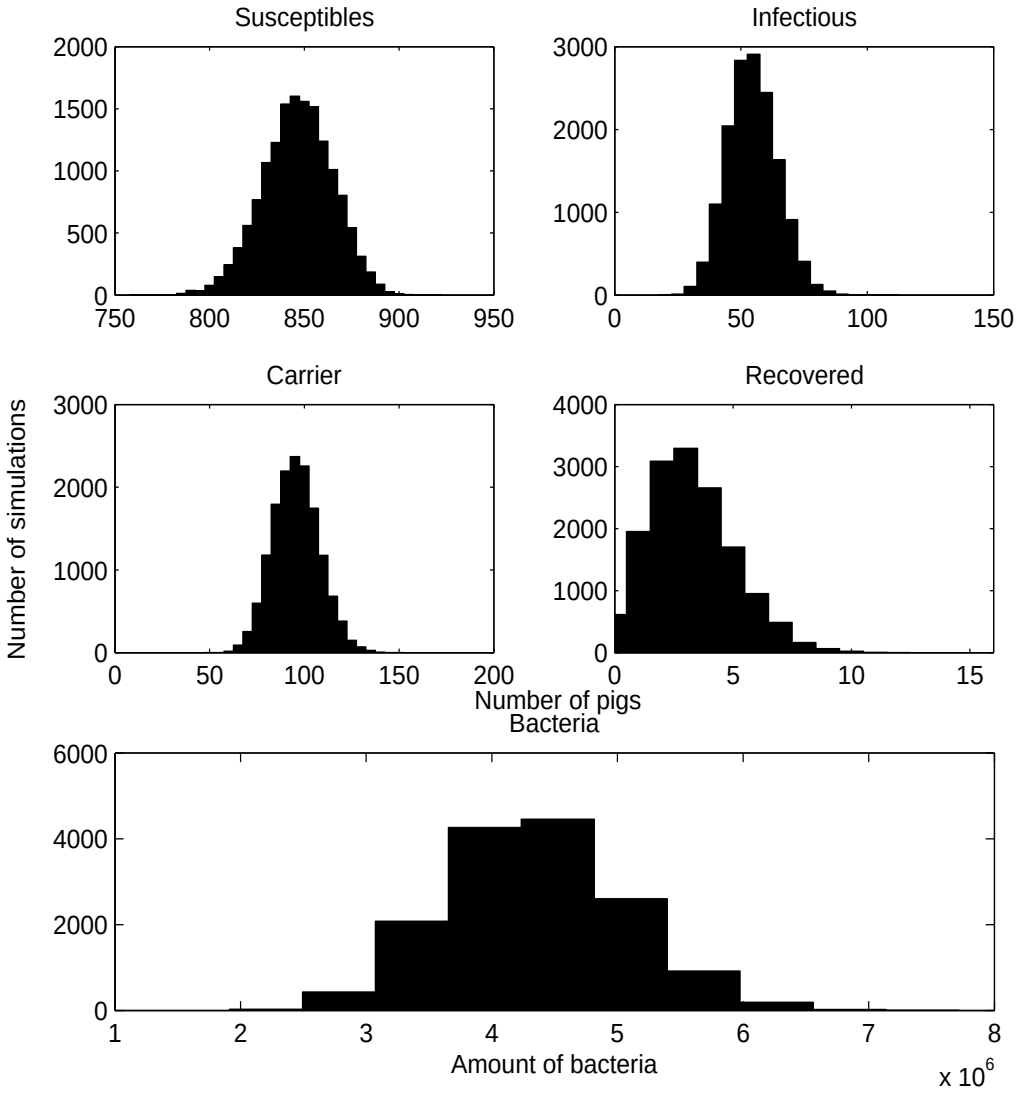

Figure 5.2: Single-roomed slatted finishing unit base result. The plots appear to be approximately normally distributed as expected, with a mean and standard deviation of 54.6 and 9.9 for infectives, and 95.6 and 12.3 for carriers.

of modelling, a real life phenomenon must be simplified in order to fully understand the model.

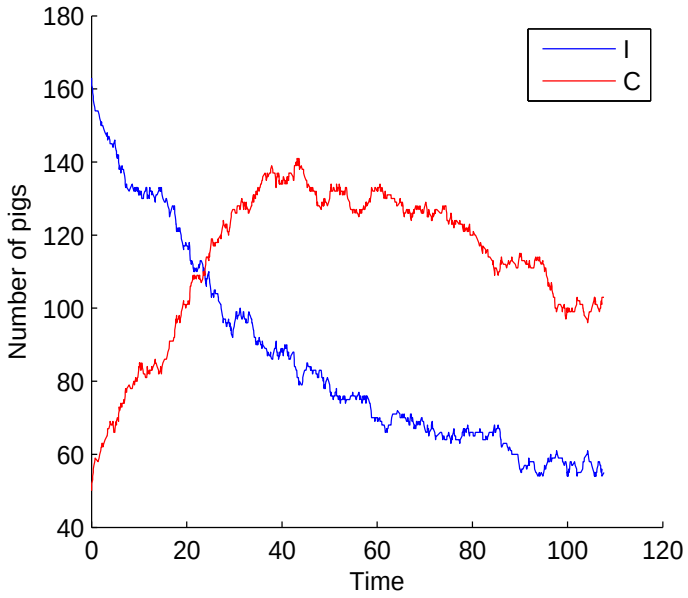

Figure 5.3: Trajectories of Infectious and Carrying pigs from a single simulation run for a single-roomed slatted finishing unit

In terms of validating the models presented here, the detailed information and data used in Chapter 4 to estimate parameter values should somewhat validate this aspect of modelling. Also, model output has been compared to the ZAP/ZNCP support visits by the VLA, which found 31 to 24% of samples positive for *Salmonella* spp. between 2005 and 2009 (Warner [2011]). Reports which found 26% of meat juice samples to be *Salmonella* positive can also be used (VLA [2007]). Furthermore, the number of infectious animals at slaughter age can be compared to a study by Davies et al. [2004] which found *S.* Typhimurium in 11.1% in caecum samples, as all parameter values (where possible) were related to *S.* Typhimurium. Therefore a realistic model output is a combined prevalence (i.e. both infectious and carrier animals) of approximately 25% (using both the abattoir and on-farm data) and an infected prevalence of approximately 11%[1]. It is important to note

[1]The validation of all models presented within the thesis, in terms of the baseline model, shall follow this form of validation.

however, that there is a lack of data with regard to the unit/farm type that samples are collected from. As such, it must be assumed that the data is consistent over all unit/farm types.

Although this model did not concur with the findings of the on-farm and abattoir sampling, it could nevertheless be deemed useful in terms of analysis of the dynamics throughout the unit. The presence of 1 local bacterial environment is thought to be insufficient in reflecting the realistic amount of bacteria that the animals are exposed to, which results in a lower *Salmonella* prevalence than expected. Although parameter values could be adjusted in order to obtain more reliable results for this model, as the parameter values fit for the structure of the forthcoming models, it did not seem sensible or appropriate to do so.

5.1.3 Calculating R_0

The basic reproduction number, R_0, is defined to be the average number of secondary infections produced when one infected individual is introduced into a host population when everyone is susceptible (for example, Hethcote [2000]). Unfortunately there was no explicit algebraic expression for R_0 for this system, and so the next generation matrix had to be investigated instead. In order to calculate this, a similar method to Xiao et al. [2005] was used, which is an extension to that of Diekmann and Heesterbeek [2000]. The mean effective infectious period, following one infection, is:

$$\frac{1}{\gamma}\left(1+\frac{\delta}{\delta+\epsilon}+\left(\frac{\delta}{\delta+\epsilon}\right)^2+\dots\right)=\frac{1}{\gamma}\left(\frac{1}{1-\frac{\delta}{\delta+\epsilon}}\right)=\frac{1}{\gamma}\left(\frac{\delta+\epsilon}{\epsilon}\right)=\frac{1}{\gamma}\left(1+\frac{\delta}{\epsilon}\right).$$

In order to calculate the mean infectious period above, the carrier state must be accounted for as carriers can return to the infectious state.

During this period, an infective in pen ni makes contacts in pen ni at rate β, and contacts pigs in pens $n(i-1)$ and $n(i+1)$ at rate α. Furthermore, bacteria are shed at rate λ. Denote by $M_{ni,mj}$ the average number of infectious contacts to pen mj made by an infective in pen ni. Therefore, the elements of the next generation matrix are:

$$\begin{aligned} M_{ni,ni} &= \frac{\beta}{\gamma}\left(1+\frac{\delta}{\epsilon}\right) + \text{indirect transmission.} \\ M_{ni,n(i-1)} &= M_{ni,n(i+1)} = \frac{\alpha}{\gamma}\left(1+\frac{\delta}{\epsilon}\right) + \text{indirect transmission.} \\ M_{ni,mj} &= \text{Indirect transmission only for } mj \notin \{n(i-1), ni, n(i+1)\}. \end{aligned}$$

The mean number of bacteria shed by one infective is $\frac{\lambda}{\gamma}\left(1+\frac{\delta}{\epsilon}\right)$, where a proportion ($prop$) remains available for consumption (local environment) and the remainder ($1-prop$) falls beneath the slats (general environment) and affects the airborne route of transmission. Each bacterium lives for an average time of $\frac{1}{l+P\kappa}$ and $\frac{1}{l+P\omega}$, within the local and general environments respectively; where P is the total number of pigs present, $P = N \times 2 \times PensPerSide$. During this time, infectious contacts in pen mj are made at rates $pN\kappa$ and $N\omega$. Therefore, the indirect transmission contribution to $M_{ni,mj}$ is $\frac{\lambda \times prop}{\gamma}\left(1+\frac{\delta}{\epsilon}\right)(pN\kappa)\frac{1}{l+P\kappa} + \frac{\lambda(1-prop)}{\gamma}\left(1+\frac{\delta}{\epsilon}\right)(N\omega)\frac{1}{l+P\omega}$. R_0 is then the maximal eigenvalue of the next generation matrix M, the entries of which are:

$$
\begin{aligned}
M_{ni,ni} &= \tfrac{\beta}{\gamma}\left(1+\tfrac{\delta}{\epsilon}\right)+\tfrac{\lambda}{\gamma}\left(1+\tfrac{\delta}{\epsilon}\right)\left[prop(pN\kappa)\tfrac{1}{l+P\kappa}+(1-prop)N\omega\tfrac{1}{l+P\omega}\right], \\
M_{ni,n(i-1)} &= \tfrac{\alpha}{\gamma}\left(1+\tfrac{\delta}{\epsilon}\right)+\tfrac{\lambda}{\gamma}\left(1+\tfrac{\delta}{\epsilon}\right)\left[prop(pN\kappa)\tfrac{1}{l+P\kappa}+(1-prop)N\omega\tfrac{1}{l+P\omega}\right] \quad \text{provided } i-1\geq 1, \\
M_{ni,n(i+1)} &= \tfrac{\alpha}{\gamma}\left(1+\tfrac{\delta}{\epsilon}\right)+\tfrac{\lambda}{\gamma}\left(1+\tfrac{\delta}{\epsilon}\right)\left[prop(pN\kappa)\tfrac{1}{l+P\kappa}+(1-prop)N\omega\tfrac{1}{l+P\omega}\right] \\
&\qquad \text{provided } i+1\leq PensPerSide, \\
M_{ni,mj} &= \tfrac{\lambda}{\gamma}\left(1+\tfrac{\delta}{\epsilon}\right)\left[prop(pN\kappa)\tfrac{1}{l+P\kappa}+(1-prop)N\omega\tfrac{1}{l+P\omega}\right] \\
&\qquad \text{otherwise } [mj\notin\{n(i-1),ni,n(i+1)\}].
\end{aligned}
$$

After analysis of the matrix M in MATLAB, the value of R_0 for this system for the selected parameters was found to be 0.7960. As R_0 was less than 1, the usual inference would be for eventual disease fade out. With the introduction of 1 infectious animal into the herd, generally the infection died out immediately, which is consistent with the low R_0 value. However, there are a number of reasons as to why this system might take longer for the operative dynamics to evolve. What must be taken into account is the presence of bacteria within the environment, which can persist in the environment for a long period, and has been shown to be present in large quantities (Figure 5.2). As such, it was thought that the presence of a bacterial environment resulted in extending the period of persistence of disease. The use of R_0 assumes that the population of each pen is infinitely large and although 25 is not particularly large, it is thought that it should be large enough to use the R_0 calculation effectively. As the system is extremely complicated, the presence of carriers also means that the infection can be sustained for a longer period of time compared to just the presence of infectious pigs. Furthermore, as there are a large number of infectious pigs at the beginning of the model, this corresponds to a large number of potential infections and therefore, even with a low R_0, could be sufficient in sustaining the infection for the duration the pigs remain within the system.

By looking at a simplified deterministic system of one pen within the model that does not account for between pen and airborne transmission (Figure 5.4), it can be seen that the deterministic model exhibits the same behaviour over the time the pigs are within the finishing unit. When run over a longer period, it can be seen that the infection does die out and therefore a low R_0 value would be expected. As this is a single group of pigs, it does not seem unreasonable to assume that extension of this deterministic system to include a number of groups and all routes of transmission, could result in a longer period of infection, so it would certainly persist for the duration prior to slaughter. Within Section 5.1.2, the model ran for the length of time typically spent in the finishing unit, which was clearly the time of interest. A simulation of the model over a longer period, showed disease to persist for a long period, but to eventually fade out.

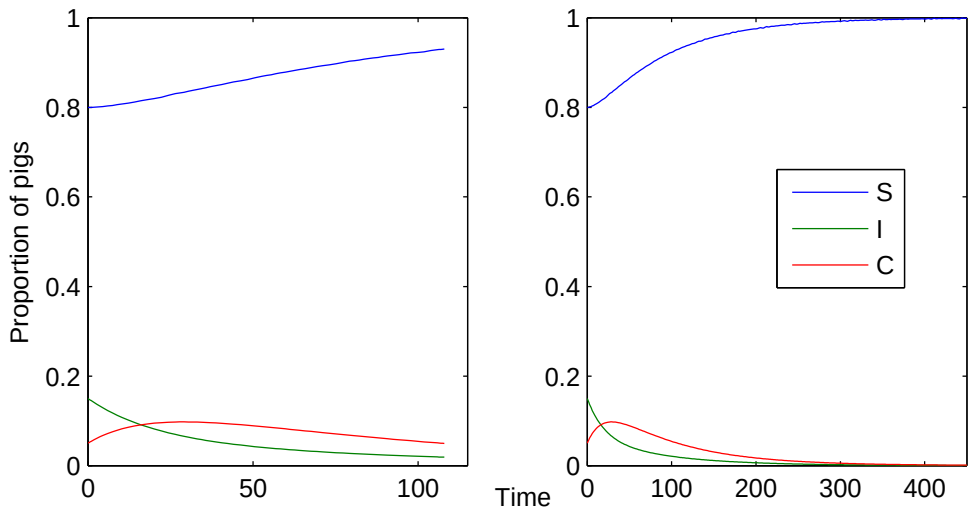

Figure 5.4: Deterministic representation of a single group on slatted flooring. Left plot shows the detail of the duration of the finishing stage (i.e. $0 \leq t \leq T_{max}$). Right plot shows long term behaviour of the model.

5.1.4 Conclusion

Within this section, the simplest model of *Salmonella* transmission around a fully slatted finishing unit was developed. Although the model was not validated in terms of end prevalence, it was thought that the model could not be fully validated due to over-simplifications within the model, as discussed previously. The model did however highlight that infection can persist on farm for a sustained period of time from infectious pigs entering the unit.

5.2 Modelling a multiple-roomed slatted unit

As mentioned previously, the structures of farms are very diverse, even within farms with similar if not identical management practices. As such, the model found in the previous section was modified to incorporate rooms, which altered the dynamics in a number of ways. It was evident from numerous farm visits that many slatted units have a tendency to have various rooms within a building; therefore this appeared to be a valid modification to make.

5.2.1 Model formulation

Clearly the previous model provided a good foundation on which to build when incorporating this changing structure. The structure of the multiple-roomed unit (Figure 5.5) was similar to that within Figure 4.1, however there were 5 pens on either side of a corridor with a fully slatted floor, within a room. Four rooms made up 1 building, and so both models could be compared directly. An SICRS/W model was used again, however 5 bacterial environments were used; i.e. 1 general environment and 1 bacterial environment per room. All rooms within a building were assumed to share the same airspace (i.e. same ventilation system) and so airborne infection was assumed to behave in the same manner

as before. A main wall that separated the rooms from each other limited the chance of cross infection between neighbouring pens.

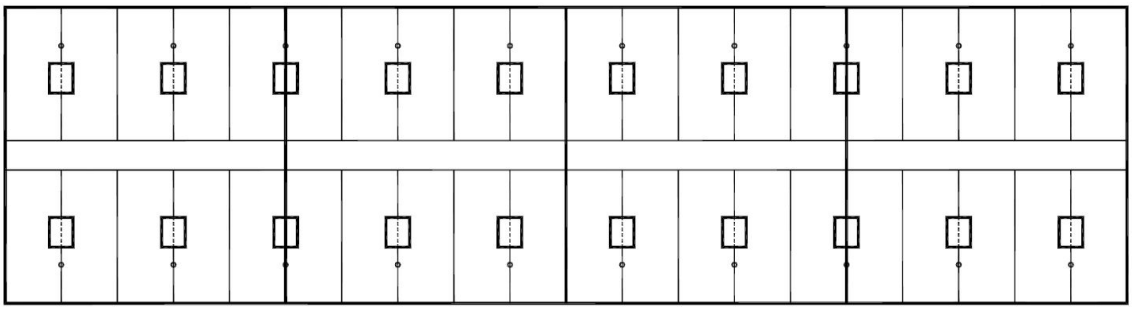

Figure 5.5: Structure of a 1000 place, multiple-roomed, fully-slatted finisher house.

In order to model the extra bacterial environments, the methodology adopted previously (Section 5.1.1) was extended as follows. Let W_g denote the bacteria in the general environment (i.e. a connection between all rooms), and $1-prop$ be the proportion of faeces that goes into the general environment. Furthermore, 4 bacterial environments relating to each individual room were present; namely W_1, W_2, W_3 and W_4. Again, suppose that $(\mathbf{S}, \mathbf{I}, \mathbf{C})$ makes a transition at time T, and that $(\mathbf{I}(\mathbf{T}), W_1(T), W_2(T), W_3(T), W_4(T), W_g(T))$ $= (\mathbf{i}, w_1, w_2, w_3, w_4, w_g)$. Also let τ be the time until the next transition of $(\mathbf{S}, \mathbf{I}, \mathbf{C})$, then each bacterial environment evolves according to:

$$\begin{aligned}
W_g(T+t) &= w_g e^{-(\omega P+l)t} + \tfrac{(1-prop)\lambda i}{\omega P+l}(1-e^{-(\omega P+l)t}),\\
W_1(T+t) &= w_1 e^{-(\kappa Rm+l)t} + \tfrac{(prop)\lambda i_1}{\kappa Rm+l}(1-e^{-(\kappa Rm+l)t}),\\
W_2(T+t) &= w_2 e^{-(\kappa Rm+l)t} + \tfrac{(prop)\lambda i_2}{\kappa Rm+l}(1-e^{-(\kappa Rm+l)t}),\\
W_3(T+t) &= w_3 e^{-(\kappa Rm+l)t} + \tfrac{(prop)\lambda i_3}{\kappa Rm+l}(1-e^{-(\kappa Rm+l)t}),\\
W_4(T+t) &= w_4 e^{-(\kappa Rm+l)t} + \tfrac{(prop)\lambda i_4}{\kappa Rm+l}(1-e^{-(\kappa Rm+l)t}),
\end{aligned}$$

where Rm is the total number of pigs within a room and $I(T+t) = (i_1, i_2, i_3, i_4)$ for $0 \leq t < \tau$.

The transitions within the multiple-roomed model can be seen in Table 5.2. Direct transmission was dealt with in a similar manner to the previous model, whereby each infective host made contacts at the points of a homogeneous Poisson process of rate β; each such contact was with a pig chosen uniformly at random from those within the same pen; if the pig contacted was susceptible, it became infectious. Similarly, infective hosts could contact pigs in neighbouring pens, within the same room, at rate α; no such contacts occur between pigs in different rooms. During its infectious period, the host shed *Salmonella* into the environment at the points of a Poisson process of rate λ. Each host, whether susceptible, infectious, carrier or recovered, consumed bacteria from the local environment according to a Poisson process with rate $\kappa W_k(t), k = 1, 2, 3, 4$; whenever a susceptible pig consumed *Salmonella*, with probability p the susceptible pig became infected. Airborne infection was again incorporated with a dependency on the general bacterial environment, which in turn allowed some form of connection between animals in all rooms. As the ventilation system used within pig housing is generally shared throughout the building, this appears to be a fair assumption.

5.2.2 Model output

A simulation of the model was run for 15,000 simulations in order to obtain an average prevalence on an infected farm, just prior to slaughter. The model found an average prevalence of $\approx 24.6\%$, where prevalence included the number of infectious and carrying pigs, with $\approx 10.2\%$ of these classed as infectious, as shown in Figure 5.6 and Figure 5.7. The number of bacteria within each room is shown in Figure 5.8.

The validity of the model appeared to be greater than the previous model, as the end

Table 5.2: Transition rates used within the slatted multiple-roomed SICRS/W model

Event	State Transition	Rate
A susceptible becomes infectious by an infective within the same pen (ni)	$(S_{ni}, I_{ni}) \rightarrow (S_{ni}-1, I_{ni}+1)$	$\frac{\beta}{N} S_{ni} I_{ni}$
An infective in pen ni ceases to infect but remains carrying *Salmonella*	$(I_{ni}, C_{ni}) \rightarrow (I_{ni}-1, C_{ni}+1)$	γI_{ni}
A carrier in pen ni starts reinfecting	$(I_{ni}, C_{ni}) \rightarrow (I_{ni}+1, C_{ni}-1)$	δC_{ni}
A carrier in pen ni recovers	$(C_{ni}, R_{ni}) \rightarrow (C_{ni}-1, R_{ni}+1)$	ϵC_{ni}
A recovered pig in pen ni becomes re-susceptible	$(S_{ni}, R_{ni}) \rightarrow (S_{ni}+1, R_{ni}-1)$	νR_{ni}
Indirect transmission from bacterial consumption, within room k[a]	$(S_{ni}, I_{ni}, W_k) \rightarrow (S_{ni}-1, I_{ni}+1, W_k-1)$	$p\kappa S_{ni} W_k$
An infectious pig from a neighbouring pen ($n(i\pm1)$)[b] infects a susceptible in pen ni, within room k	$(S_{ni}, I_{ni}) \rightarrow (S_{ni}-1, I_{ni}+1)$	$\frac{\alpha}{N} S_{ni} I_{n(i\pm1)}$
Indirect transmission via the airborne route	$(S_{ni}, I_{ni}, W_g) \rightarrow (S_{ni}-1, I_{ni}+1, W_g-1)$	$\omega S_{ni} W_g$
Bacteria are shed into the general environment	$(W_g) \rightarrow (W_g+1)$	$(1-prop)\lambda \sum_{n,i} I_{ni}$
Removal of bacteria from the general environment after airborne infection	$(W_g) \rightarrow (W_g-1)$	$\omega(\sum_{ni}(I_{ni}+C_{ni}+R_{ni}))W_g$
Bacteria are shed into the local (room) environment	$(W_k) \rightarrow (W_k+1)$	$prop\lambda \sum_{n,i\in k} I_{ni}$
Death of bacteria	$(W_x)^c \rightarrow (W_x-1)$	lW_x
Consumption of bacteria by infectious, carrier and recovered pigs	$(W_k) \rightarrow (W_k-1)$	$\kappa(\sum_{n,i\in k}(I_{ni}+C_{ni}+R_{ni}+(1-p)S_{ni}))W_k$

Note: Only state elements that are affected by the corresponding event are shown.
The full set of state elements is $\{(S_{ni}, I_{ni}, C_{ni}, R_{ni}) : n = 1, 2; i = 1, 2..., PensPerSide\}, (W_g, W_1, W_2, W_3, W_4)$.

[a] for $k = 1, 2, 3, 4$

[b] if $n(i \pm 1)$ in same room as ni

[c] where $x \in \{1, 2, 3, 4, g\}$

Note: Within room 1, $i \in \{1, 2, 3, 4, 5, 21, 22, 23, 24, 25\} = M_1$
Within room 2, $i \in \{6, 7, 8, 9, 10, 26, 27, 28, 29, 30\} = M_2$
Within room 3, $i \in \{11, 12, 13, 14, 15, 31, 32, 33, 34, 35\} = M_3$
Within room 4, $i \in \{16, 17, 18, 19, 20, 36, 37, 38, 39, 40\} = M_4$

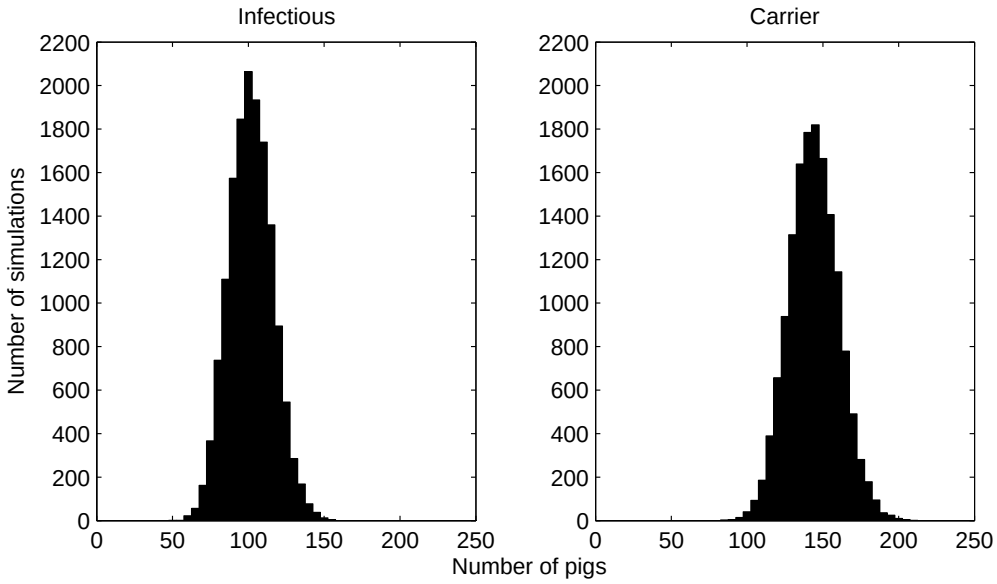

Figure 5.6: Multiple-roomed slatted finishing unit base result. The plots appear to be approximately normally distributed as expected, with a mean and standard deviation of 101.7 and 9.9 for infectives, and 143.95 and 16.3 for carriers.

prevalence and the proportion of infectious pigs prior to slaughter are in line with the on farm studies, which found 31% to 24% of samples positive for *Salmonella* spp. between 2005 and 2009 (Warner [2011]). Furthermore, the model predicted approximately 10.2% of pigs to be shedding the bacteria, which is within the confidence interval within the study by Davies et al. [2004] which found *S.* Typhimurium in 11.1% of caecum samples (95% CI: 9.8 - 12.3).

The results obtained from this model differ from those obtained from the single-roomed counterpart in Section 5.1.2. It was originally thought that the introduction of rooms would result in a decrease in prevalence due to the reduction in contact between neighbouring pens. It would appear however that the introduction of rooms has resulted in an increase in the amount of bacteria available due to a decrease in the number of exposed

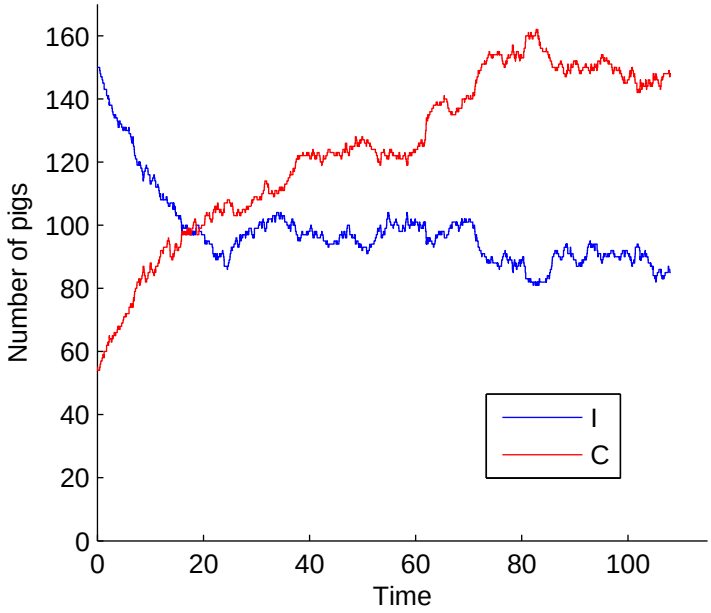

Figure 5.7: Trajectories of Infectious and Carrying pigs from a multiple-roomed slatted finishing unit

animals within the environment. Consequently, an increase in prevalence was observed.

Within the slatted units, there was an increase in prevalence when rooms were incorporated into the system. However, what was of particular interest, was the considerable increase in prevalence, despite only a small increase in R_0, as shown in the forthcoming section (Section 5.2.3). As such, there appears to be a change in the dynamics, which is not readily explained by such a small increase in R_0. The bacterial environment has been shown to be a key aspect, and it was thought that changes in the environments has played a key role in changing the dynamics. Within the single roomed unit, there was a slightly slower, but more sustained reduction in the number of infectious animals (Figure 5.3) compared to a more self-limiting reduction within the multiple roomed unit (Figure

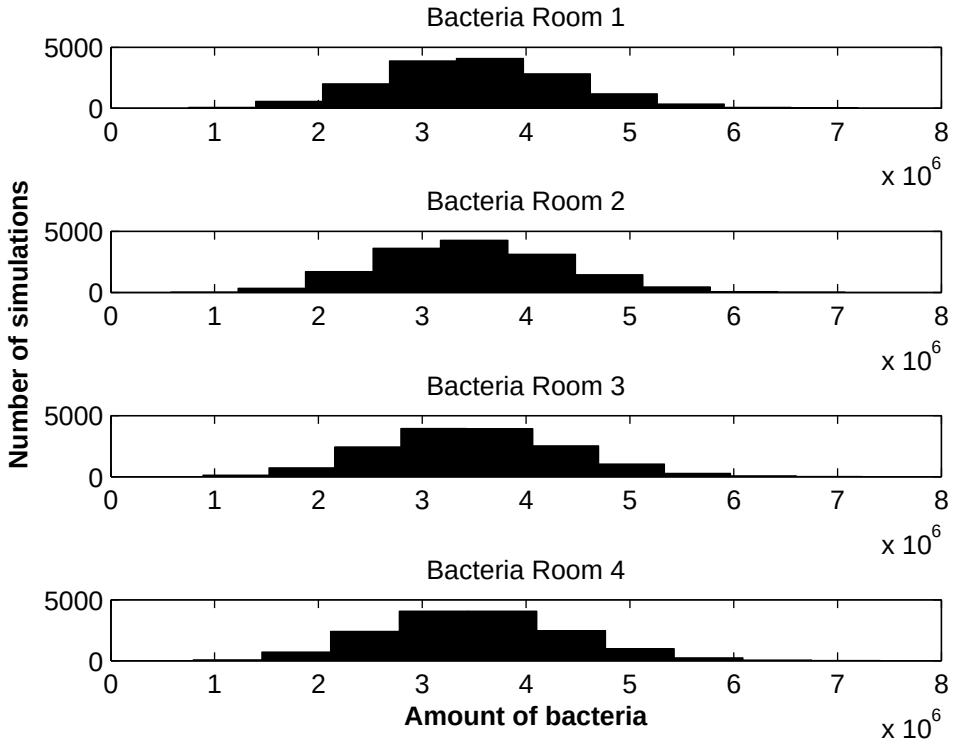

Figure 5.8: Multiple-roomed slatted finishing unit bacteria base result. The plots appear to be approximately normally distributed as expected.

5.7). This could be due to the speed of the uptake of infection via faecal consumption, whereby the single roomed system has a higher uptake. The mean number of bacteria within the local environments within both models were quite similar (Figures 5.2 and 5.8), however a key difference is the number of animals exposed to this bacteria. With fewer animals present within one environment (multiple room), there was less eating, which resulted in a slower use of the infection bank within the environment. This adds further to the idea that the environmental pool of bacteria, becomes a pool of deferred infection, and consequently, has a low effect on the value of R_0, but can be influential in changing the system dynamics.

5.2.3 Calculating R_0

R_0 can be calculated for this system in a similar manner to the previous calculations of Section 5.1.3. The mean number of bacteria shed by one infective is $\frac{\lambda}{\gamma}\left(1+\frac{\delta}{\epsilon}\right)$, where a proportion (*prop*) remains available for consumption (local environment) and the remainder $(1-prop)$ is under the slats (general environment) and affects the airborne route of transmission. Each bacterium lives for an average time of $\frac{1}{l+R\kappa}$ and $\frac{1}{l+P\omega}$, within the local and general environments respectively, where R is the number of pigs within a room and P is the total number of pigs present. During this time, infectious contacts in pen mj are made at rates $pN\kappa$ and $N\omega$. Therefore, the indirect transmission contribution to $M_{ni,mj}$ is $\frac{\lambda\times prop}{\gamma}\left(1+\frac{\delta}{\epsilon}\right)(pN\kappa)\frac{1}{l+R\kappa}+\frac{\lambda(1-prop)}{\gamma}\left(1+\frac{\delta}{\epsilon}\right)(N\omega)\frac{1}{l+P\omega}$. R_0 is then the maximal eigenvalue of the next generation matrix M, the entries of which are:

$$
\begin{aligned}
M_{ni,ni} &= \frac{\beta}{\gamma}\left(1+\frac{\delta}{\epsilon}\right)+\frac{\lambda}{\gamma}\left(1+\frac{\delta}{\epsilon}\right)\left[prop(pN\kappa)\frac{1}{l+R\kappa}+(1-prop)N\omega\frac{1}{l+P\omega}\right], \\
M_{ni,n(i\pm1)} &= \frac{\alpha}{\gamma}\left(1+\frac{\delta}{\epsilon}\right)+\frac{\lambda}{\gamma}\left(1+\frac{\delta}{\epsilon}\right)\left[prop(pN\kappa)\frac{1}{l+R\kappa}+(1-prop)N\omega\frac{1}{l+P\omega}\right] \\
&\qquad \text{provided } i\pm1 \text{ is in the same room as } i, \\
M_{ni,mj} &= \frac{\lambda}{\gamma}\left(1+\frac{\delta}{\epsilon}\right)\left[prop(pN\kappa)\frac{1}{l+R\kappa}+(1-prop)N\omega\frac{1}{l+P\omega}\right] \\
&\qquad \text{otherwise.}
\end{aligned}
$$

The R_0 value for this system was 0.8204. Again, as R_0 was less than 1, the disease would have been expected to die out. The same results as found in Section 5.1.3 also apply here.

5.3 Discussion

This chapter developed novel models describing farming methodologies that have not previously been modelled. Also, the techniques used within these models have not been

applied to modelling *Salmonella* transmission in pigs. The previous models that assess *Salmonella* control on farm use discrete time models (Hill et al. [2007], Ivanek et al. [2004], Lurette et al. [2008], Soumpasis and Butler [2009]), however the models presented here use a continuous time methodology in order to try and heighten realism. The use of semi-stochastic models in modelling disease transmission has been previously used for bacterial infections in other animal species (Xiao et al. [2006], Turner et al. [2006]), but has not been applied to pigs. The use of this modelling methodology allows the detailed analysis of how the bacterial environment can evolve and ensures a fast and efficient use of coding and simulation.

Fully slatted finishing houses are generally split into rooms as discussed within Section 5.2. The results obtained from this model are plausible, given the prevalence data that was available. Furthermore, this is the only known study to calculate the basic reproduction number, R_0, for a system that models *Salmonella* dynamics in pigs, which identifies some interesting findings. An analysis of R_0 showed a low value (< 1), however, even with a low R_0 value, it was found that infection could persist on farm for a sustained period with a number of infectious pigs entering the unit.

Salmonella epidemiology in pigs has been widely studied (Lo Fo Wong et al. [2002], Berends et al. [1996], van Duijkeren et al. [2002]), however the epidemiology can differ between farm practices and when external factors (e.g. transport, fomites) have some effect. With regard to farm practice, it has been shown that the feed and feeding system used on farm (Lo Fo Wong et al. [2002], van der Wolf et al. [1999], Lo Fo Wong et al. [2004]), the structure of pens, continuous flow stocking and receiving pigs from more than

3 suppliers (Lo Fo Wong et al. [2004], Nollet et al. [2005], Farzan et al. [2006]) are risk factors. As such, a different model has been developed in order to assess how the structure of pens affects the *Salmonella* epidemiology (Chapter 7). External factors such as birds and rodents have also been shown to be risk factors in the spread of *Salmonella* (Lo Fo Wong et al. [2002]). These have not been included within the model presented, however this has been discussed in more detail in Chapter 9. *S.* Typhimurium has been shown to be the most predominant serovar in pigs over a number of years (for example van Duijkeren et al. [2002]). Consequently, the model aims to describe the transmission of this particular serovar. Although it appears as though this serovar is dominant within the environment, it is possible that other serovars are present on farm with a much lower effect.

Farm studies tend to focus on a small population of pigs rather than an entire farm, likely due to costs. In such studies, an artificially high amount of bacteria is used to infect the animals and so the epidemiology that is seen within these studies may not reflect the epidemiology within the whole unit (Gray et al. [1995, 1996a], Wood et al. [1989]). The study by Kranker et al. [2003] that follows groups of pigs within an infected Danish herd, found shedding to rise in the nursery (up to 60 days old) and subsequently declined during finishing. Although the model presented here does not establish any initial increase in shedding, the time point at which the model begins is close to the end of the observed period of increased shedding. The finding that the number of infectious animals decreases during the finishing stages of production however supports the trend found within the model simulation (Figure 5.3 and 5.7).

The aim of the work within this chapter was to develop a model that provides an

insight into the *Salmonella* dynamics on a pig unit. The development of these models allows the analysis of the sensitivity of the parameters used within these models. As the results of the models were plausible, it was possible to identify and test certain practical interventions that could be applied, and see whether this had any effect on *Salmonella* prevalence, as done in Chapter 6.

Chapter 6

Slatted unit interventions

This chapter shall investigate interventions implemented on the slatted-floored unit as described in Chapter 5. Rather than analysing specific interventions, the possible modes of action of interventions shall be investigated. Furthermore, the concept of thresholds shall be analysed.

It is important to note that only the results of interventions that could be implemented were analysed, as testing interventions that could not be implemented in reality would be futile.

6.1 Initial prevalence

Salmonella on farm clearly has to be initiated somehow. Within the models presented here, the prevalence at slaughter was dependent on the initial number of infected animals, both infectious and carriers. With the average number of infected pigs entering the unit (20%), a prevalence at slaughter of approximately 24.6% was found. With varying levels of infectious pigs entering the unit, it was shown that prevalence just prior to slaughter increased until approximately 60% of pigs entering the unit were infectious (Figure 6.1);

after which, any increase in the initial proportion of infectious pigs entering the unit had little effect on prevalence at slaughter.

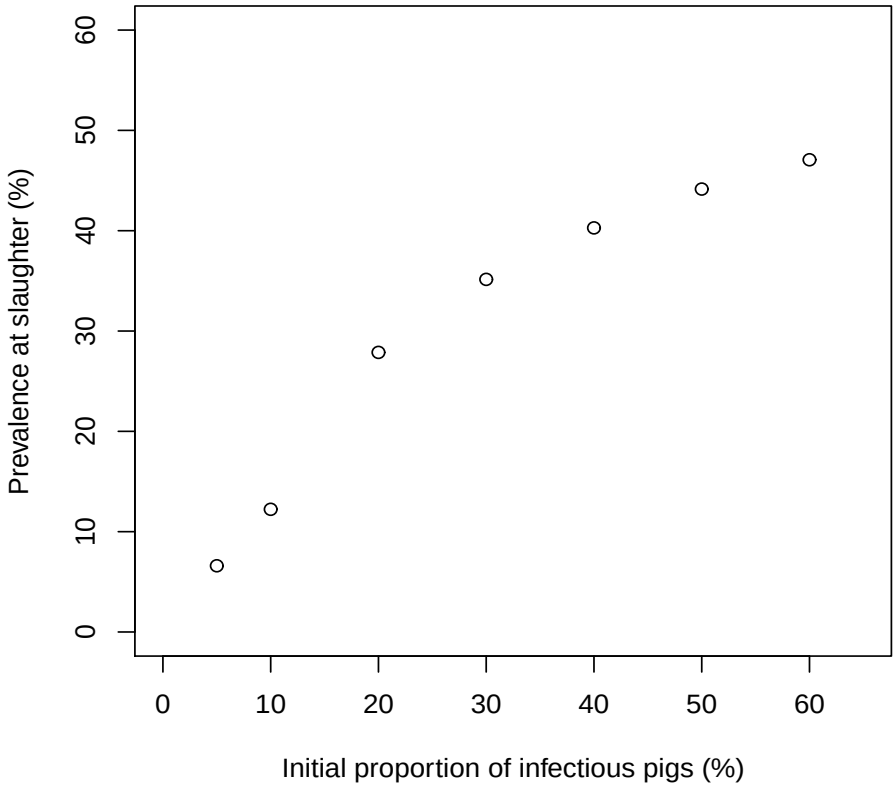

Figure 6.1: Mean prevalence level prior to slaughter with varying numbers of initial infectious pigs entering the unit

Simulations also showed that if low numbers of infectious animals enter the unit, then *Salmonella* either becomes eradicated (when levels are extremely low; i.e. $< 1\%$) or maintained at low levels. It is important to note however that this assumed that no other form of infection exists. As such, this result should be taken on the side of caution, as

a low number of infectious animals entering the unit may not be sufficient to ensure a low *Salmonella* prevalence, as external factors may cause an additional number of pigs to become infected.

6.2 Probability of infection after *Salmonella* exposure

One possible mode of action for *Salmonella* intervention is to reduce the probability of becoming infected after *Salmonella* exposure, which is something that could possibly be achieved via vaccination. With the standard parameter value ($p = 2.3 \times 10^{-6}$), a prevalence of 24.6% was found. A 10 times reduction in this parameter resulted in a prevalence of approximately 7.82%. A 100 times reduction resulted in a prevalence of a similar order. Conversely, a 10 times increase from baseline resulted in a prevalence of approximately 91.15%. There is a potential implication here that there exists a range of infectious doses between 10^5 and 10^7 cfu, over which the effective probability of infection (i.e. $p\kappa SW$) changes significantly.

The data used to calculate the probability of infection following exposure within Chapter 4 showed that 10^6 cfu was the lowest dose required in order for pigs to become infected. The main problem with the majority of studies that take place are the artificially high amounts of bacteria given to the pigs (oral inoculation of up to 10^9 cfu). Simulations showed that changes in this parameter could result in large increases in prevalence. Since the value of p was estimated using the typical infectious dose, model behaviour could be related to this dose. With an increase in the parameter value, a lower dose is required in order to cause an infection. Consequently, the probability of infection following exposure can be seen as a key driver of *Salmonella* transmission.

6.2.1 The effect of a change in probability of infection on R_0

Clearly the probability of infection after *Salmonella* exposure had a major affect on *Salmonella* prevalence, which should have a corresponding effect on the basic reproduction number, R_0. When the probability of infection is decreased 10 times, the corresponding R_0 value was 0.1432, hence suggesting a reduction in prevalence compared to the base result as found in Section 5.2, where $R_0 = 0.8204$.

The significantly large increase in prevalence when the probability of infection was 10 times higher was reflected in the R_0 value, jumping to 7.59. Clearly this R_0 value was greater than 1 and thus an outbreak would be expected. This increase in R_0 as the value of p increases is shown in Figure 6.2.

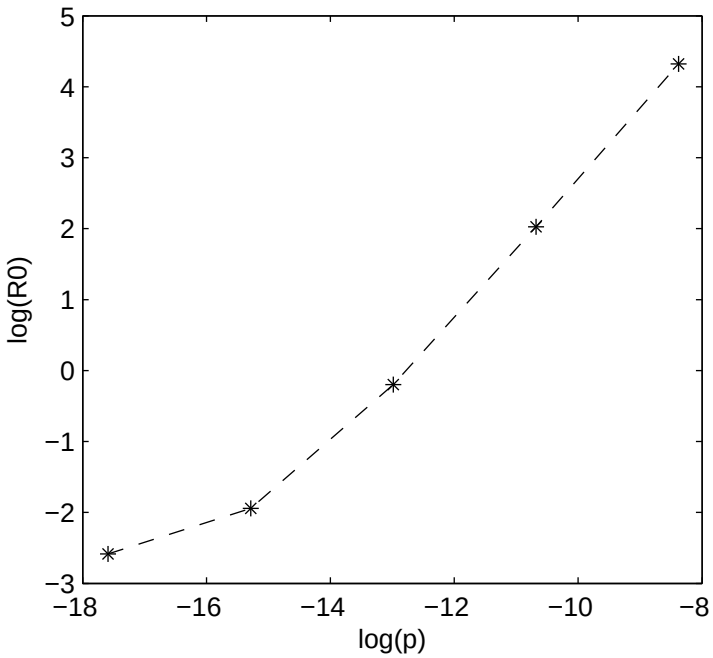

Figure 6.2: Graph highlighting the effect of the probability of infection (p) on R_0. Natural logs were used, with base parameter $\log(p) = -12.98$.

6.3 Rate of reversion to infectiousness

It is well known that any increased stress on pigs that are infected but not shedding (defined as carrier pigs within the models) could cause the animal to resume shedding the bacteria in the faeces. Clearly the majority of stress would be imposed during transport to the abattoir and during lairage, however the general movement of pigs on farm could also have an effect. Within the models, it has been assumed that minimal stress is imposed on the animals on farm (corresponding to "infrequent reversion" in figure 6.3); however, a hypothetical stresser which causes the animals to resume shedding was shown to influence *Salmonella* prevalence (Figure 6.3).

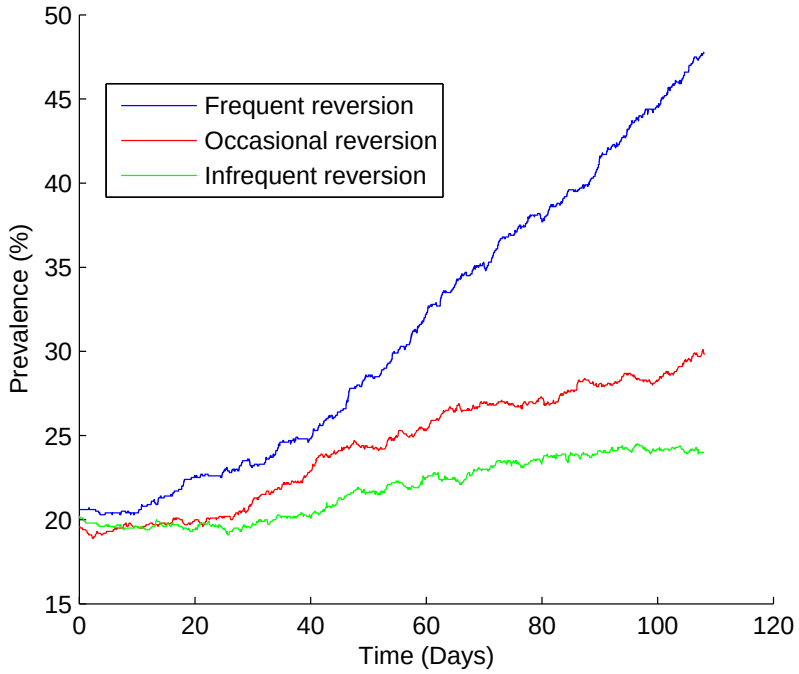

Figure 6.3: Effect of the rate of reversion to infectiousness (δ) on *Salmonella* prevalence. Note: $\delta = \frac{1}{14}$ for frequent reversion, $\delta = \frac{1}{61}$ for occasional reversion and $\delta = \frac{1}{108}$ for infrequent reversion.

Interestingly, when animals occasionally resumed shedding ("occasional reversion", after a mean of approximately 60 days), the value of R_0 became greater than 1 (≈ 1.05) and animals frequently resuming shedding ("frequent reversion") caused R_0 to increase to ≈ 2.79 (Figure 6.4); which became apparent with the large increase in final prevalence (Figure 6.3). As such, it was important that stress or any other cause for animals to continually resume shedding was minimised in order to keep prevalence as low as possible.

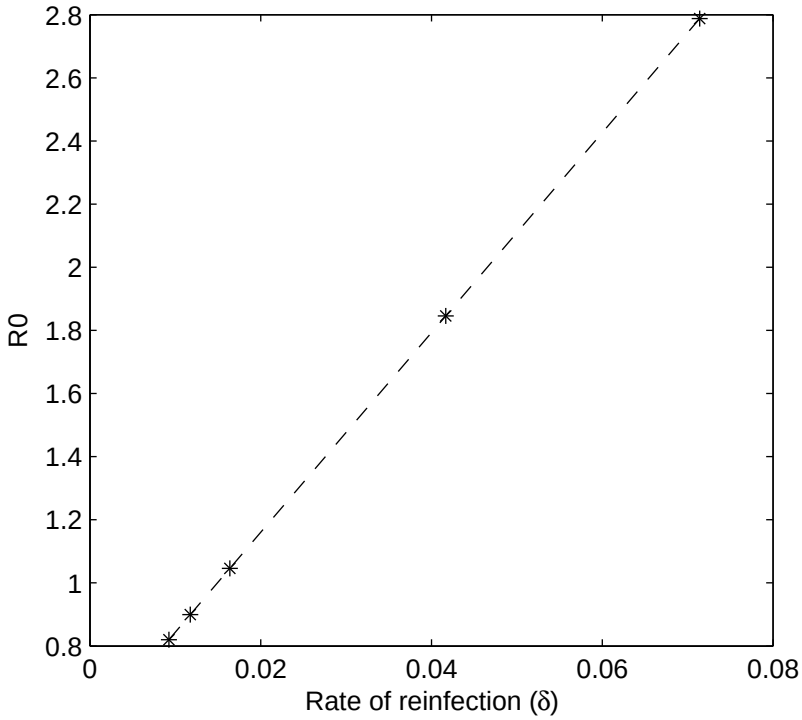

Figure 6.4: Graph highlighting the effect of the rate of reversion to infectiousness (δ) on R_0. Base parameter value of $\delta = 0.01$.

6.4 Duration of excreting and carrying the bacteria

A possible intervention that could be analysed within the model was the effect of the mean duration of excreting and carrying the bacteria on *Salmonella* prevalence. As shown in

Figure 6.5, prevalence decreases linearly as the duration of excreting and carrying the bacteria decreases. The mean duration of excreting *Salmonella* appeared to have the biggest effect on prevalence, but nevertheless seemed to have less effect than interventions tested previously.

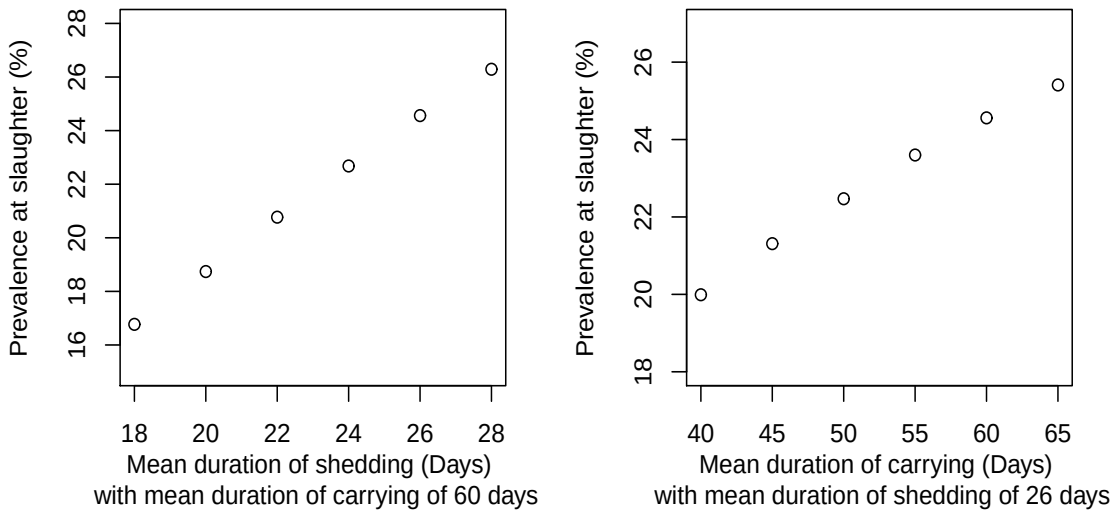

Figure 6.5: Prevalence level with varying durations of excreting and carrying *Salmonella*

It is perhaps not surprising that the duration of shedding had a greater effect on reducing *Salmonella* prevalence, as this resulted in reducing the time an animal remained infectious. The sensitivity analysis performed on these durations clearly had to remain within a plausible interval. However, even if the duration of carrying the bacteria was reduced to the potential minimum time (40 days), more than a third of the entire duration of the finishing stage would be spent as infected. By applying both interventions with the best possible durations (i.e. reducing the duration of excreting and carrying to 18 and

40 days, respectively), a small decrease in the R_0 value was observed ($R_0 \approx 0.5$), most of which was attributable to the reduction in the shedding period, with an average *Salmonella* prevalence at slaughter age of $\approx 12\%$. Interestingly, applying these modifications to the simple deterministic system as shown in Figure 5.4, showed very little change to the dynamics, which highlights the low sensitivity of the model to these parameters.

It can be seen that a decrease in the duration of shedding and carrying the bacteria resulted in a decrease in the value of R_0 (Figure 6.6). However, the duration of shedding was found to have a greater effect, which concurs with previous findings.

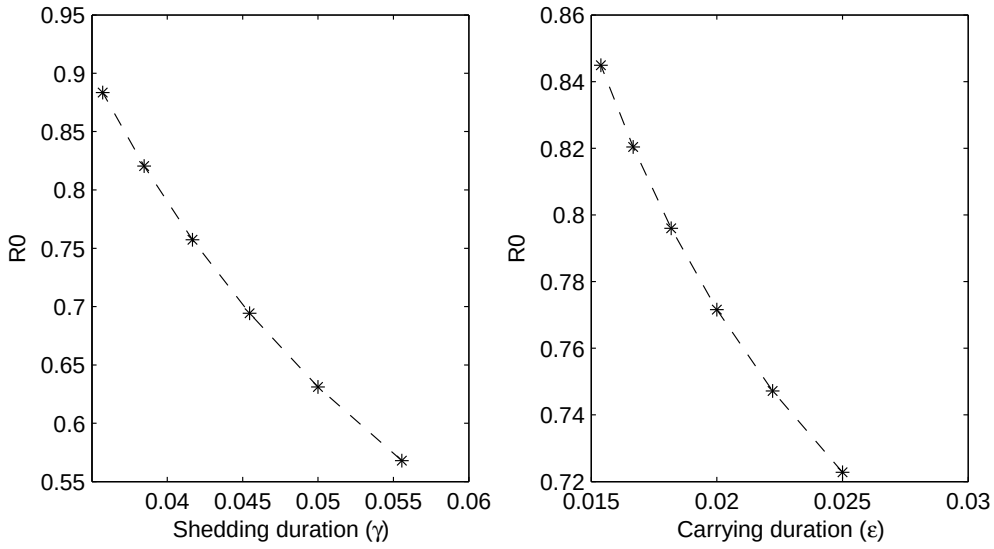

Figure 6.6: Graph highlighting the effect of the shedding duration (left) and carrying duration (right) on R_0. Base parameter of $\gamma = 0.039$ and $\epsilon = 0.017$.

6.5 Shedding rate and "super-shedders"

The presence of *Salmonella* in the environment is thought to be extremely important in sustaining on-farm prevalence. As such, the amount of bacteria shed in the faeces is an

important factor within the spread of *Salmonella*; i.e. the shedding rate, λ. Within the multiple-roomed fully-slatted unit, with a 10 times higher shedding rate, the average prevalence at the end of the finishing stage was found to be $\approx 91.2\%$ (as shown in Figure 6.7) compared to a prevalence of 24.6% with a normal shedding rate.

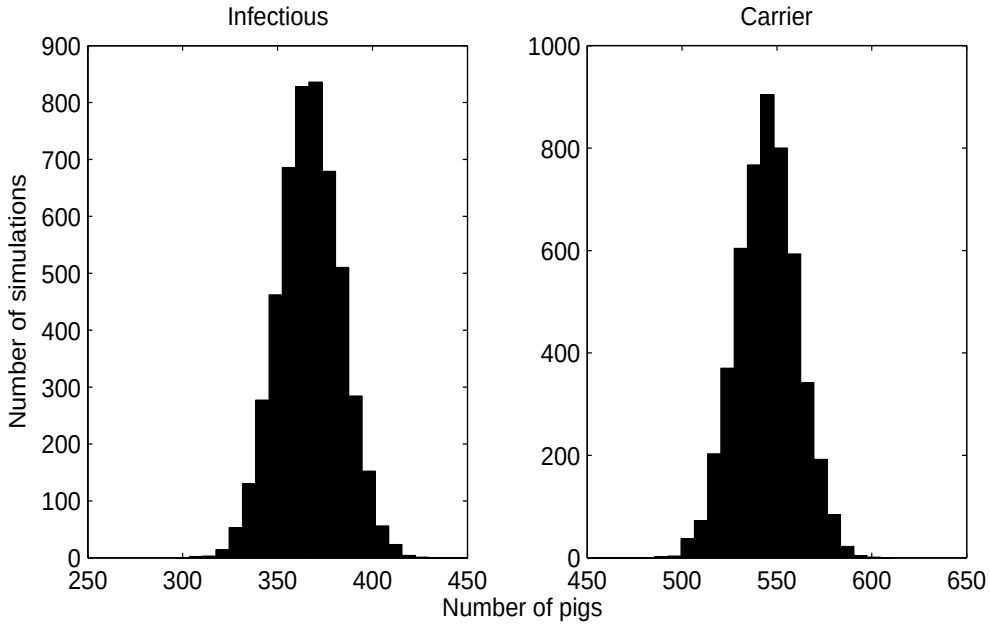

Figure 6.7: The effect of a 10-fold increase in shedding rate on *Salmonella* prevalence on a 1000-place, multiple-roomed, fully-slatted unit. A histogram showing the distribution of numbers of infectious and carrier animals present at slaughter.

This indicated that farms with a high *Salmonella* prevalence could be due to the presence of a number of pigs shedding high numbers of bacteria, otherwise known as "super-shedders." The way in which the model was formulated did not allow the analysis of individual pigs within the farm; therefore, the additional shedding could be due to a large number of pigs shedding medium levels of bacteria, or a low number of pigs shedding high numbers of bacteria as previously suggested.

Clearly the way in which "super-shedders" have been modelled was not ideal. By increasing the shedding rate (λ) it assumes the average shedding rate is increased for all animals. To some extent this does allow for the presence of "super-shedders" as the average shedding rate would see an increase. In order to model "super-shedders' more explicitly, an additional status would need to be incorporated into the model, which would allow for the increase in shedding. This however would add further complications as the extent to which "super-shedders" are present on farm is unknown. Consequently, for the aims of this study, it was thought that the way "super-shedders" were modelled was the best way of exploring their presence without complicating the model. Arguably however, as the model dynamics appear to be driven by the bacterial environment, explicitly modelling "super-shedders" is not necessary.

6.5.1 The effect of higher shedding on R_0

As the prevalence was significantly higher with increased shedding, the basic reproduction number, R_0, should account for this increase in prevalence by becoming larger than 1. When the amount of bacteria shed was increased, the R_0 calculation used within Section 5.2.3 found an R_0 value of 7.5970. It can be seen that as the shedding rate increases, the value of R_0 also increases (Figure 6.8). As a result of the increase in R_0, *Salmonella* infection was able to spread and persist within the environment, both when a number of infectious pigs entered the unit and when 1 infectious pig entered the unit. In order to model the full effects of introducing 1 infectious animal into the unit, the single-roomed unit was used. When 1 infectious animal, shedding large numbers of bacteria, was introduced into a single-roomed unit, infection was able to spread with the number of infectious and carrying animals increasing, with no sign of reaching equilibrium within the finishing

stage (Figure 6.9).

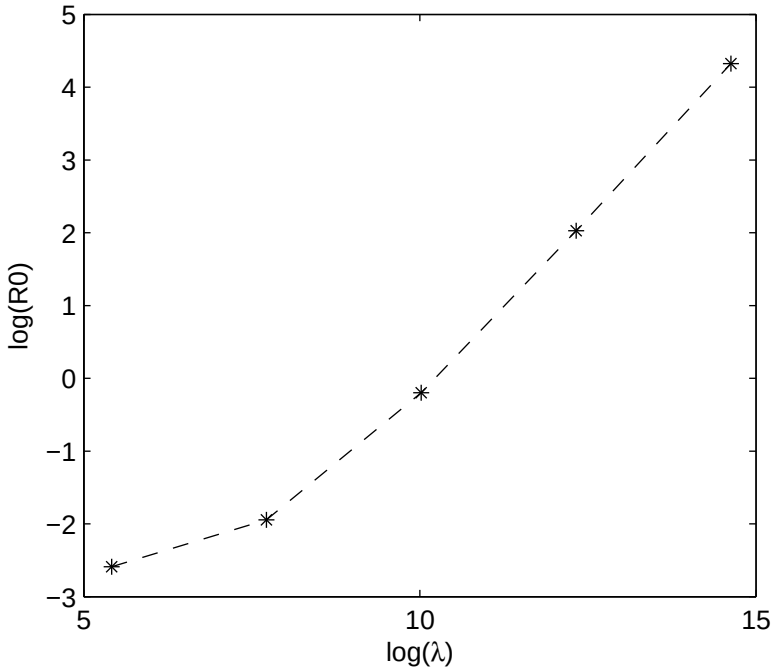

Figure 6.8: Graph highlighting the effect of the shedding rate (λ) on R_0. Natural logs were used, with base parameter $\log(\lambda) = 10.02$.

6.5.2 Interventions implemented on a multiple-roomed, fully-slatted unit with the presence of a number of "super-shedding" pigs

The finding that a number of pigs shedding high numbers of *Salmonella* in their faeces could have such a drastic affect on prevalence is important. As such, a key issue would be to analyse interventions that could have an effect on disease spread even with this high rate of shedding. As shown in Figure 6.7, with the introduction of "super-shedders" randomly spread throughout the unit, prevalence became approximately 90%. However, if all infectious pigs were contained within 1 room of the building (Figure 6.10) then in general, this could be enough to halt transmission as infection was unable to spread throughout

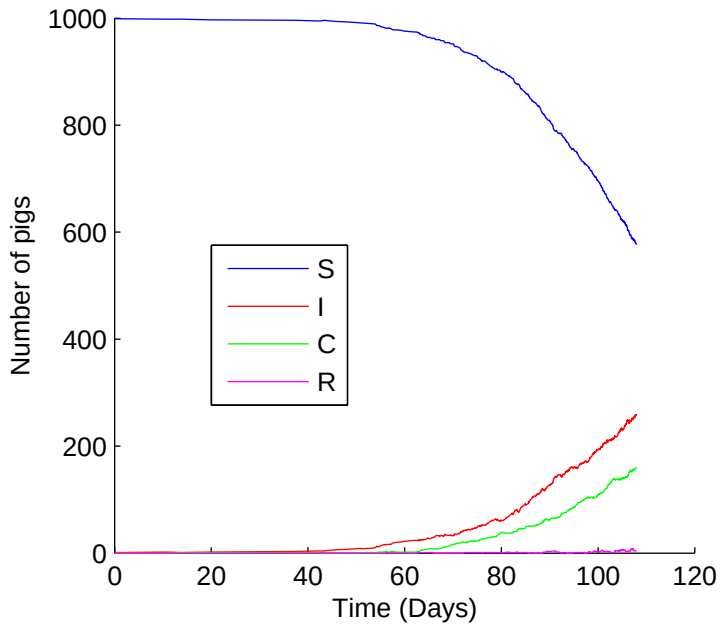

Figure 6.9: One simulation plotting the trajectories of S, I, C and R when 1 highly infectious pig was introduced into a single-roomed, fully-slatted finishing unit

the whole unit. As such, containing all infectious animals to 1 room limited the number of animals that were exposed to the bacteria and consequently limited *Salmonella* transmission. Although farmers cannot easily identify individual pigs that become infected, this finding could still be exploited by attempting to keep pigs in groups of pens with solid divisions; thus ensuring every effort is made to prevent contact between pens and essentially create different epidemiological groups.

Clearly it is not easy to identify all infected animals in order to contain the infection due to many animals being asymptomatic. However, if the assumption that carrying animals are incapable of passing on the infection is true, a focus on containing infectious pigs (i.e. those animals that are shedding the bacteria) should be taken. As long as

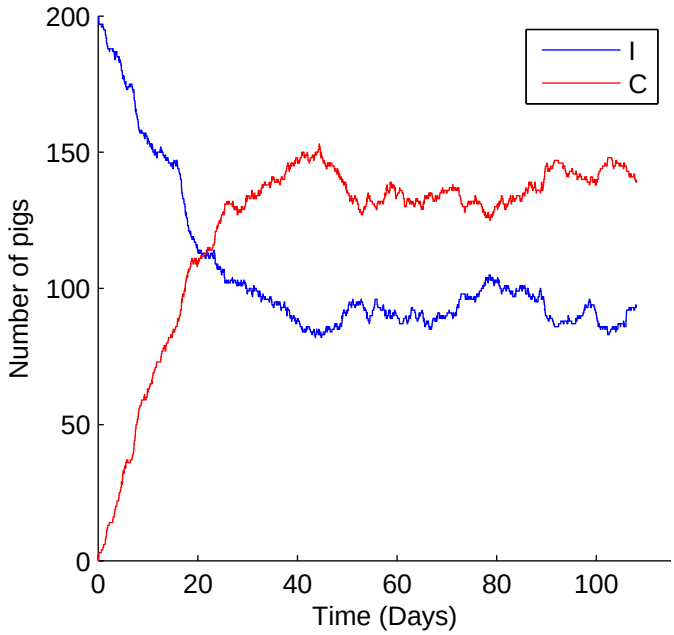

Figure 6.10: One simulation showing the result of containing infectious pigs shedding high numbers of bacteria within 1 room of a multiple-roomed, fully-slatted finishing unit

stress on farm is minimised (i.e. carrying animals rarely become re-infectious) then the presence of animals carrying the bacteria elsewhere in the unit could have a minimal effect.

The probability of infection was found to be an important parameter when shedding was at normal levels. When shedding was high, a 10-fold reduction in the probability of infection saw *Salmonella* prevalence reduce to 24.56 % (Figure 6.11); a reduction in prevalence of approximately $\frac{2}{3}$. This indicated that the probability of becoming infected after *Salmonella* exposure was an important factor in disease spread, not only when shedding was at normal levels, but was able to lower the effects when shedding was high.

When a pig becomes infected, the animal generally sheds the bacteria in the faeces for

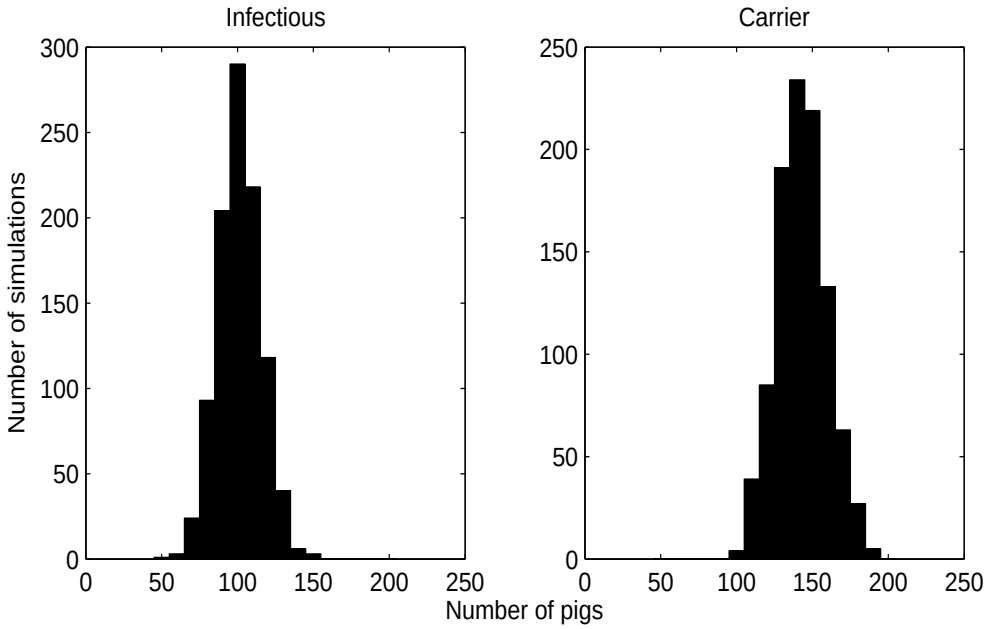

Figure 6.11: Proportion of infectious and carrying animals when the probability of infection is reduced

at least 14 days. A sensitivity analysis was performed, in which the duration of shedding appeared to have little impact on *Salmonella* prevalence (prevalence of approximately 87% when shedding was reduced to 18 days). In order to test how effective interventions targeting the duration of shedding could be, a simulation of the model was performed when the duration of shedding was reduced to 4 days. This was found to have some effect with prevalence reducing to approximately 49%. However, such a large reduction in the duration of shedding may not be plausible.

When shedding was higher, the initial proportion of infectious animals entering the farm had a much lower effect on prevalence. Although Figure 6.9 showed that the introduction of 1 infectious animal could cause an epidemic within the single-roomed model, within the multiple-roomed unit this would not have the same effect due to the large

effects arising from the use of rooms (as highlighted in Figure 6.10). However, when infection was randomly spread throughout the unit, as little as 1% of infectious animals entering the unit could induce an outbreak (simulation of the model showed an average prevalence at slaughter of approximately 83%). Further simulations of the model showed a consistent *Salmonella* prevalence whether 5% or 45% of infectious pigs entered the unit. Consequently, efforts that aim to minimise prevalence prior to this stage of production may not be the most effective use of resources.

It was previously shown that when animals frequently resume shedding (increase in δ to $\delta = \frac{1}{14}$) could result in an increase in prevalence. However, when shedding was higher, it was shown that the rate of resuming shedding had a much lower effect on *Salmonella* prevalence prior to slaughter (Figure 6.12). With the higher shedding, the R_0 value for animals infrequently resuming shedding $\left(\delta = \frac{1}{108}\right)$ was found to be ≈ 7.60 and become progressively higher as the rate of resuming shedding increases. Although R_0 increases, it was thought that the value was large enough to have a small affect on prevalence, which was highlighted by simulation.

The main effect of animals reverting to infectiousness with high shedding was found to relate to the relative proportions of animals that were classed as infectious and those classed as carriers (Figure 6.13). Animals infrequently and occasionally resuming shedding displayed similar behaviour with regard to the dynamics of infectious and carrying animals. When animals frequently resumed shedding however, the dynamics were very different, which resulted in the presence of a large number of infectious animals. As a large proportion of the population were infected, the presence of a large number of infectious

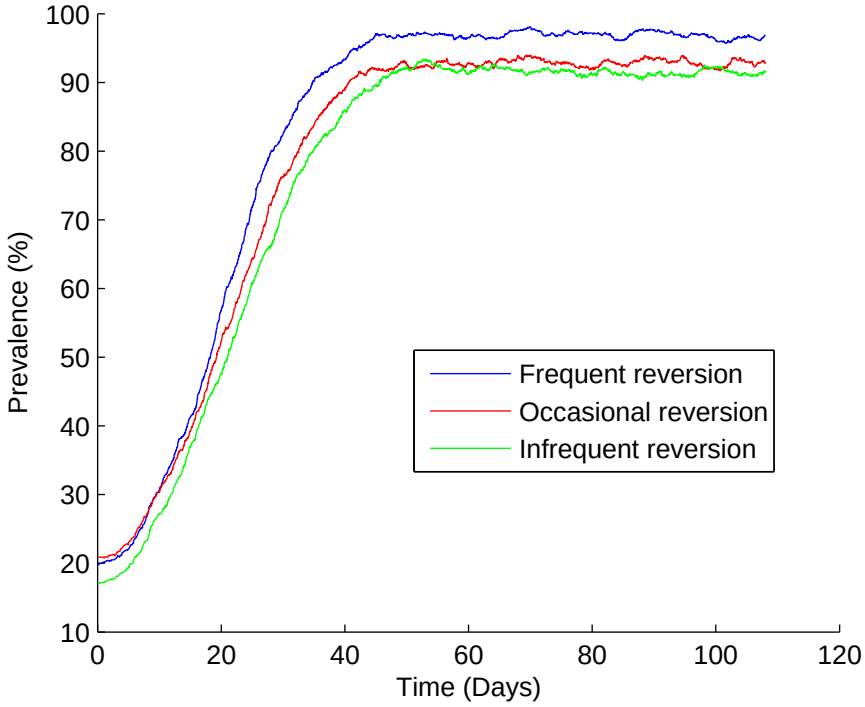

Figure 6.12: Effect of the rate of reversion to infectiousness (δ) on *Salmonella* prevalence when shedding was high ($\lambda = 2.25 \times 10^5$). Note: $\delta = \frac{1}{14}$ for frequent reversion, $\delta = \frac{1}{61}$ for occasional reversion and $\delta = \frac{1}{108}$ for infrequent reversion.

pigs had little effect. When shedding was at normal levels, animals frequently re-shedding had a greater effect as a larger proportion of the population were susceptible to infection (Figure 6.3).

6.6 Discussion

This chapter investigated interventions implemented on the fully-slatted unit developed in Chapter 5, in an attempt to highlight possible modes of action that result in a decrease or control of *Salmonella* prevalence on farm.

The amount of bacteria shed once a pig becomes infectious was found to be of great

importance. Various studies have previously established the existence of super shedders in other animal populations (for example *E. coli* O157 in cattle, Matthews et al. [2006], Arthur et al. [2010]), and proved that such animals have an important role in the transmission dynamics. Although such animals have not yet explicitly been proved to exist within the pig population, the distribution of *Salmonella* shedding in pigs is large (Gray et al. [1995, 1996a], Smith and Jones [1967], Gutzmann et al. [1976], Scherer et al. [2008]). As such, it is not unreasonable to conclude that some pigs shed higher numbers of bacteria than others, and would therefore be classed as "super-shedders." The finding that higher shedding (and therefore the likely presence of "super-shedders") is important for the industry as it highlights the need for an intervention to address this issue.

Another factor that had a major impact on prevalence was the probability of infection after *Salmonella* exposure. It appeared that there was a range of sensitivity whereby an infectious dose of greater than 10^6 cfu resulted in a high prevalence, whereas lower than 10^6 cfu resulted in some form of control of *Salmonella*. This range of sensitivity was an important finding since relatively little effort can have a big effect, but beyond a certain point any further effort is inconsequential. A decrease in the probability of infection following exposure was also found to be extremely influential in *Salmonella* control even when shedding was at high levels.

Clearly there needs to be a practical application for these interventions to be effective. Although the amount of bacteria shed and the probability of infection following exposure are unique parameters, and play an important role in the dynamics in their own right, they are connected. If shedding is high, then consequently the effective probability of

infection (i.e. $p\kappa SW$) increases due to the high number of bacteria available within the environment. As such, it is quite possible that an intervention targeting one aspect could inadvertently affect both scenarios. It has been shown that adding antibiotics to feed can reduce the amount of *Salmonella* shed by an infected animal (Gutzmann et al. [1976]). However, it is important to note that this finding only saw a reduction in the amount shed as opposed to the ability of the bacteria to colonize the animal. However, problems arise with the presence of resistant *Salmonella* strains, whereby addition of the antibiotic to the resistant *Salmonella* strain can increase the quantity, duration and prevalence of faecal shedding Williams et al. [1978]. As the level of antimicrobial resistance in pig isolates is high Davies et al. [2004], it is possible that the use of antibiotics could increase *Salmonella* risk. Consequently, the use of antibiotics has the potential for increasing as well as reducing *Salmonella* risk. As such, an analysis of the cost effectiveness of applying this intervention would need to be investigated as well as consideration of the implications of antimicrobial usage in the food chain.

The addition of prebiotics to drinking water has been shown to be associated with a reduction in *S.* Typhimurium shedding. Probiotics on the other hand have been shown to have little effect on shedding, but do show signs of reducing the presence of the bacteria internally (in the mesenteric lymph nodes for example), which implies that probiotics and prebiotics could alter the gut microflora composition to the benefit of the animal (Letellier et al. [2000]). Acidification of feed has been shown to inhibit *Salmonella* growth, which results in a reduction in infection levels and consequently the amount of bacteria shed (Blanchard and Kjeldsen [2003]). However, the type of food used could also have some impact on the dynamics, for example wet feed has been associated with a reduction in

shedding (Blanchard and Kjeldsen [2003]). Clearly there are a number of possible interventions that could be implemented with regard to feed, however a large factor for decision making is cost. In changing the whole system to use wet feed, it is quite possible that a large scale renovation of the unit would need to occur, which is consequently less likely to be implemented.

It would be interesting to see if vaccination would have an effect on both aspects by decreasing the amount of bacteria shed when an animal becomes infected and/or reducing the susceptibility of the animals. Various vaccines have been developed (for example Salmoporc (IDT BIOLOGIKA) licensed live vaccine) but are not widely used on farm. It is quite possible that vaccination is scarcely used due to the potential for the vaccine to interfere with current control programs relying on serology (Selke et al. [2007]). Vaccination against viral infections is expected to limit the chance of bacterial infections (Potter et al. [2008]) and should aim to prevent colonisation of the host and minimise the shedding of the pathogen (Rostagno [2011]). A number of studies have been conducted that show vaccination is associated with a reduction in isolation of *Salmonella* in slaughter weight pigs with a reduction of clinical symptoms and colonization of the animal (Denagamage et al. [2007], Selke et al. [2007], Schwarz et al. [2011]).

The effect of stress on *Salmonella* dynamics highlighted some interesting behaviour. When shedding was at normal levels, animals continually resuming shedding was found to have a large effect on *Salmonella* prevalence, and consequently R_0. However, with high shedding, animals resuming shedding has a much lower effect. Tasks such as the movement of animals increase the amount of stress imposed on them (Lo Fo Wong et al.

[2002]). This increase in stress has been shown to increase susceptibility to infection and levels of faecal shedding of *Salmonella* (Callaway et al. [2006]), however the increase in the number of *Salmonella* positive pigs does not stay sustained for a long period (Nollet et al. [2005]). Consequently, stress should be kept to a minimum, particularly so when *Salmonella* infection is not widespread.

It was also shown that transmission could be halted if infectious pigs were contained early enough when shedding was high. Although this did not guarantee infection would not spread throughout the unit, the majority of the time saw the infection contained. Although the identification of infected animals is difficult, should any advances in identifying such animals arise, an intervention of this nature is one that would be relatively easy to apply in practice.

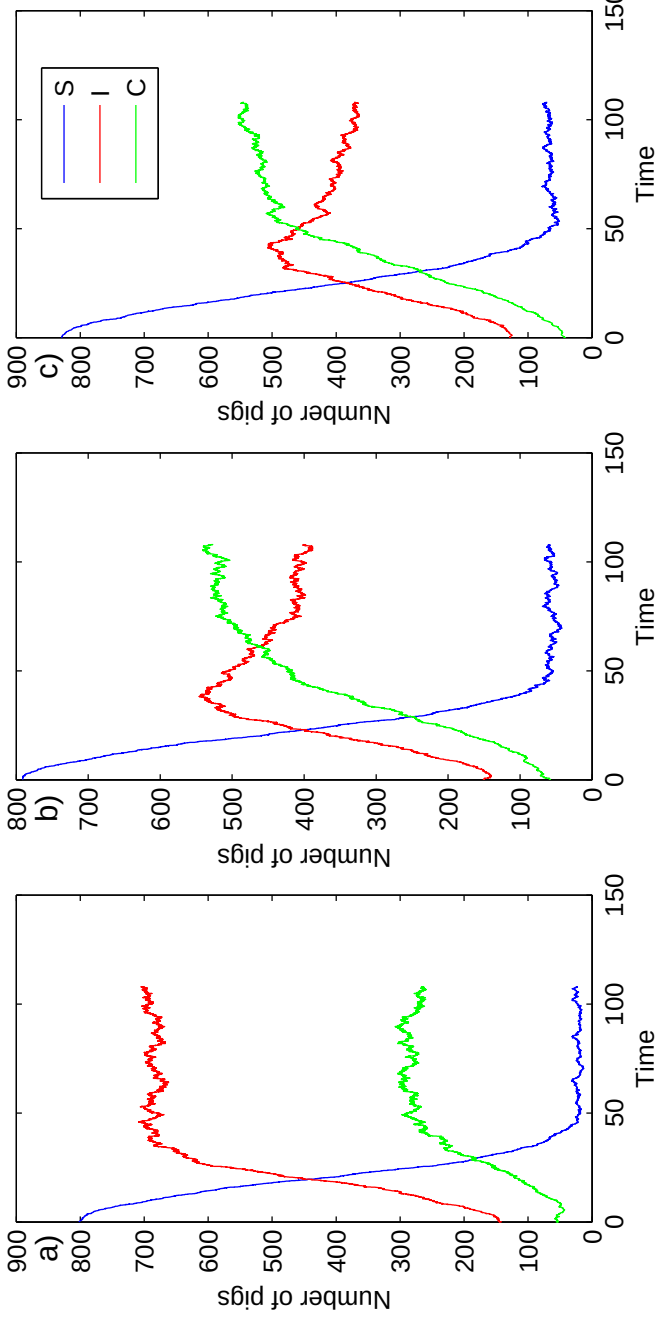

Figure 6.13: Differentiation between *Salmonella* status with varying rates of reversion. Note: a) frequent reversion, b) occasional reversion and c) infrequent reversion

Chapter 7

Modelling *Salmonella* spread within a solid-floored unit

Another type of pig unit used within the UK is a solid-floored unit. As this will have differences compared to the models described in Chapter 5, a model describing this new structure shall be completed in order to compare differences in *Salmonella* dynamics.

7.1 Model formulation

Again a susceptible - infected - carrier - recovered - susceptible (SICRS) model incorporating environmental bacteria was developed. In this model, there were 12 possible events (see Table 7.1), as well as regular cleaning. The effect of cleaning was to immediately reduce the number of bacteria present in the environment. Thirteen parameters were used as described in Chapter 4, namely the number of pigs per pen N, the number of pens on either side of a corridor $PensPerSide$, the direct infection rate β, the airborne infection rate ω, the rate at which a pig ceases to be infectious γ, the rate at which a carrier becomes re-infectious δ, the rate at which a pig ceases to carry the bacteria ϵ, the loss of immunity rate ν, the bacterial consumption rate κ, the shedding rate λ, the bacteria death rate l, the cross infection rate α and the indirect infection probability p. All parameters were

assumed to be strictly positive. The total number of animals on farm is denoted by P. An additional parameter was used within the model to account for cleaning, namely the proportion of faeces that remains after cleaning q.

The structure of the unit itself (see Figure 4.2) was again acquired from BPEX [2006]; 2 rows of pens lie centrally within a building, with a solid division between each row. A scraping passage runs along either side of the building, which corresponds to each row of pens. Gates separate the pens along this scraping passage, resulting in the possibility of infection via direct contact between pigs in neighbouring pens, with rate parameter α. Airborne transmission was also a factor within the spread of *Salmonella* transmission, which was assumed to be dependent on the amount of bacteria within the environment, with rate parameter ω. As there was solid flooring, any bacteria shed were available for consumption; i.e. $prop = 1$. It was assumed that pens were cleaned out on a weekly basis, which was assumed to be 90% efficient, therefore 10% of faeces remained present after scraping; i.e. $q = 0.1$.

Again, all pigs enter and leave the farm at the same time; i.e. pigs enter the model at $t = 0$ and leave at $t = T_{max}$. Furthermore, it was assumed that there was no mixing of pigs, and so all pigs remain within the same pen until time T_{max}. The amount of bacteria within the environment evolved in the same manner as in Section 5.1.1. Suppose (S, I, C) makes a transition at time T, and that $(I(T), W(T)) = (i, w)$. Let τ be the time until the next transition of (S, I, C) then:

$$W(T+t) = we^{-(\kappa P+\omega P+l)t} + \frac{\lambda i}{\kappa P+\omega P+l}(1 - e^{-(\kappa P+\omega P+l)t}), 0 \leq t < \tau. \tag{7.1}$$

Table 7.1: Transition rates used within the solid-floored SICRS/W model

Event	State Transition	Rate
A susceptible becomes infected by an infective within the same pen (ni)	$(S_{ni}, I_{ni}) \rightarrow (S_{ni}-1, I_{ni}+1)$	$\frac{\beta}{N} S_{ni} I_{ni}$
An infective in pen ni ceases to infect but remains carrying *Salmonella*	$(I_{ni}, C_{ni}) \rightarrow (I_{ni}-1, C_{ni}+1)$	γI_{ni}
A carrier in pen ni starts reinfecting	$(I_{ni}, C_{ni}) \rightarrow (I_{ni}+1, C_{ni}-1)$	δC_{ni}
A carrier in pen ni recovers	$(C_{ni}, R_{ni}) \rightarrow (C_{ni}-1, R_{ni}+1)$	ϵC_{ni}
A recovered pig in pen ni becomes re-susceptible	$(S_{ni}, R_{ni}) \rightarrow (S_{ni}+1, R_{ni}-1)$	νR_{ni}
Indirect transmission from bacterial consumption	$(S_{ni}, I_{ni}, W) \rightarrow (S_{ni}-1, I_{ni}+1, W-1)$	$p\kappa S_{ni} W$
An infected pig from a neighbouring pen ($ni \pm 1$) infects a susceptible in pen ni	$(S_{ni}, I_{ni}) \rightarrow (S_{ni}-1, I_{ni}+1)$	$\frac{\alpha}{N} S_{ni} I_{n(i\pm1)}$
Indirect transmission via the airborne route	$(S_{ni}, I_{ni}, W) \rightarrow (S_{ni}-1, I_{ni}+1, , W-1)$	$\omega S_{ni} W$
Bacteria shed into the environment	$(W) \rightarrow (W+1)$	$\lambda \sum_{n,i} I_{ni}$
Death of bacteria	$(W) \rightarrow (W-1)$	lW
Removal of bacteria from the environment after airborne infection	$(W) \rightarrow (W-1)$	$\omega(\sum_{n,i}(I_{ni}+C_{ni}+R_{ni}))W$
Consumption of bacteria by infected, carrier and recovered pigs	$(W) \rightarrow (W-1)$	$\kappa(\sum_{n,i}(I_{ni}+C_{ni}+R_{ni}+(1-p)S_{ni}))W$

Note: Only state elements that are affected by the corresponding event are shown.
The full set of state elements is $\{(S_{ni}, I_{ni}, C_{ni}, R_{ni}) : n = 1, 2; i = 1, 2..., PensPerSide\}, W$.

However, as it was assumed the unit was cleaned out on a weekly basis, equation 7.1 only remains valid over the whole of the interval $[T, T+\tau]$ if the transition time T and the proposed next transition time $T+\tau$ are not separated by a week boundary (i.e. on day 7, 14 etc). Suppose instead that the next week boundary after T occurs at time b, and that $T+\tau > b$. Then the amount of bacteria within the environment immediately prior to cleaning, $W(b-)$, is evaluated using equation 7.1 with $t = b - T$. The amount of bacteria immediately after cleaning is then computed as $W(b+) = qW(b-)$. The whole process is then re-started from time b. That is, a new proposed event time is generated. On each week boundary, the bacteria evolution changes according to:

$$W(T+t) = q\left(we^{-(\kappa P+\omega P+l)t} + \frac{\lambda i}{\kappa P+\omega P+l}(1-e^{-(\kappa P+\omega P+l)t})\right) \tag{7.2}$$

7.2 Model output

A simulation of the model was run for 15,000 simulations in order to obtain an average prevalence on an infected farm, just prior to slaughter. The model found an average prevalence of $\approx 25.4\%$, where prevalence includes the number of infected and carrying pigs, with $\approx 10.0\%$ of pigs classed as infected and excreting, as shown in Figure 7.1. Furthermore, the amount of bacteria left prior to slaughter was found to be $\approx 5 \times 10^7$ cfu, which was higher than that within the slatted models. This was to be expected since any bacteria shed by an infectious animal were left within the animals immediate environment.

A plot of a trajectory (Figure 7.2) showed similar behaviour to the slatted models presented in Chapter 5, whereby the number of carriers remained consistently higher than infected pigs. The dynamics of the bacterial population showed that cleaning behaved in

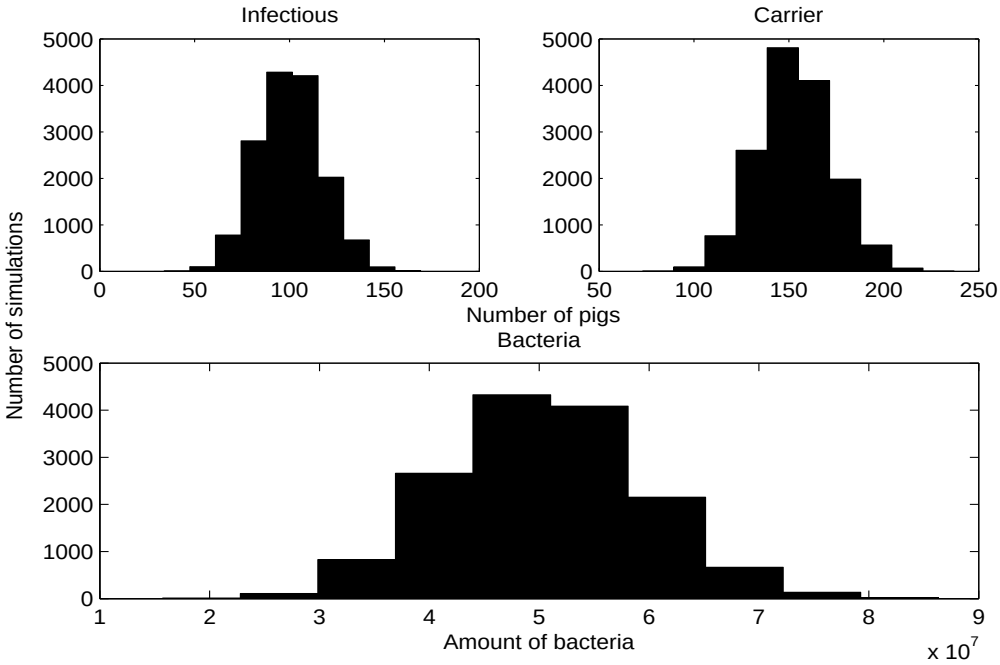

Figure 7.1: Solid-floored finishing unit base result. The plots appear to be approximately normally distributed as expected, with a mean and standard deviation of 100.5 and 16.9 for infectives, and 153.2 and 19.7 for carriers.

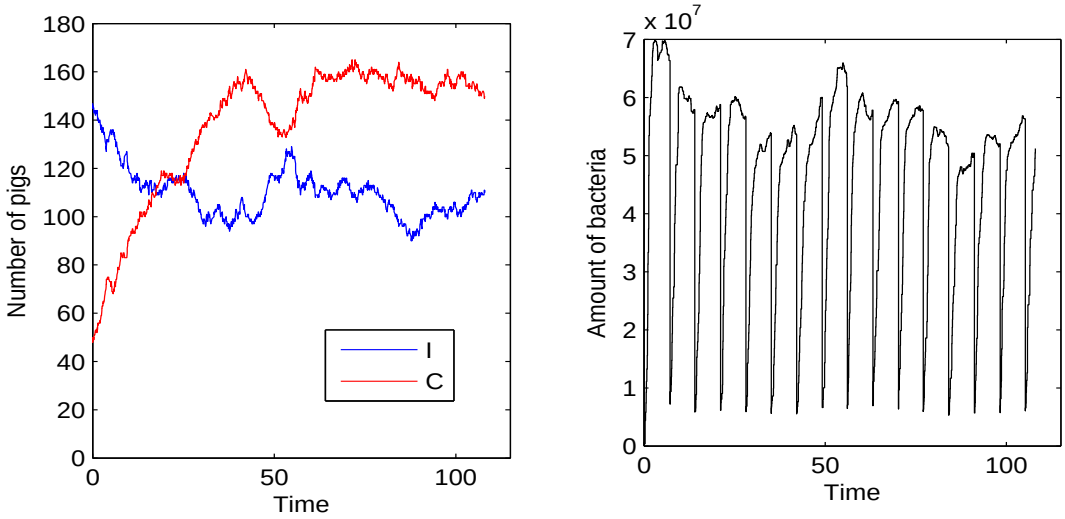

Figure 7.2: Trajectories of numbers of infectious pigs, carrying pigs (left) and bacterial population dynamics (right) from a single simulation run for a solid-floored finishing unit

the correct manner, whereby the amount of bacteria fell to 10% of its value at the end of the week for the duration of the cycle.

7.3 Discussion

This chapter developed the first model that explicitly models a unit with this type of structure. The changes made to the structure of the unit itself were valid as a number of farms within the UK have this type of unit during the finishing stages of production, which was also evident within Chapter 2. A significant difference built within this model was the weekly cleaning of the unit. Consequently, it was the first model that can explicitly take into account the effects of cleaning and disinfection on a unit.

The model predicted a prevalence that was within the range that was plausible in reality. Unfortunately there was no information regarding unit structure within the abattoir study (DEFRA [2006a]) regarding prevalence. As such, it had to be assumed that the prevalence was an average over all farm structures. However, the model could still be analysed for various on-farm interventions in order to assess which intervention has the greatest effect on *Salmonella* transmission. A number of interventions are imposed on the model developed here, and analysed within Chapter 8. The basic reproduction number, R_0, was not calculated for this model, due to the incorporation of cleaning and disinfection, which was thought to cause added complications within the calculations.

Chapter 8

Solid unit interventions

This chapter shall investigate interventions implemented on the solid floored unit as described in Chapter 7. Similar interventions that were implemented in Chapter 6 shall be adopted here also in order to analyse the difference in dynamics between the different styled units.

8.1 Cleaning and disinfection

Cleaning and disinfection is clearly an important aspect of on farm management practice, especially with regard to biosecurity. Furthermore, it is a highly intensive process and requires a large amount of time to be done efficiently. The Farm Tool Questionnaire (Chapter 2) suggested a number of biosecurity practices were required for the attainment of a low *Salmonella* prevalence. As the model incorporates cleaning and disinfection, it enabled the testing of this aspect of biosecurity on on-farm prevalence. Within the model, the efficiency of cleaning could be analysed by analysis of the parameter q; the proportion of faeces that remained present after cleaning. As such, a farm that cleaned to a good standard could remove 90% of the bacteria from the environment for example, compared to a farm with poor cleaning that only removed 10% of the bacteria (Figure 8.1).

The model showed that fully effective cleaning alone was not enough to eradicate *Salmonella* once infection was established. However the prevalence was lower if cleaning took place on farm (Figure 8.1), which implied that cleaning and disinfection was still a worthwhile task. This concurs with a study by Erdman et al. [2005] which found that cleaning and disinfection reduces environmental bacteria but fails to eradicate *Salmonella* on farm. Furthermore, some on-farm work by the VLA found improved cleaning and disinfection on farm translated into a reduction in prevalence of approximately 10% (Armstrong [2010]). The model predicted a reduction in prevalence of approximately 8%, which seemed a relatively good estimate for this effect.

8.2 Initial prevalence

Salmonella was introduced into the model by the initial number of infected animals entering the unit. By varying the initial proportion of infectious animals that enter the unit, the way in which this affects *Salmonella* prevalence prior to slaughter could be analysed. After simulation of the model, it was found that *Salmonella* prevalence increased until 60% of pigs entering the unit were infected (Figure 8.2). There was little effect on prevalence at slaughter if more than 60% of pigs were infected when introduced into the unit, which shows similar behaviour to the results from the slatted unit (Figure 6.1).

Although both models exhibit similar behaviour with regard to the initial proportion of pigs that are infectious (Figure 6.1 and 8.2), subtle differences can be observed. Within the solid unit, for values $> 30\%$ the observed prevalence at slaughter was found to be lower than the corresponding prevalences within the slatted unit.

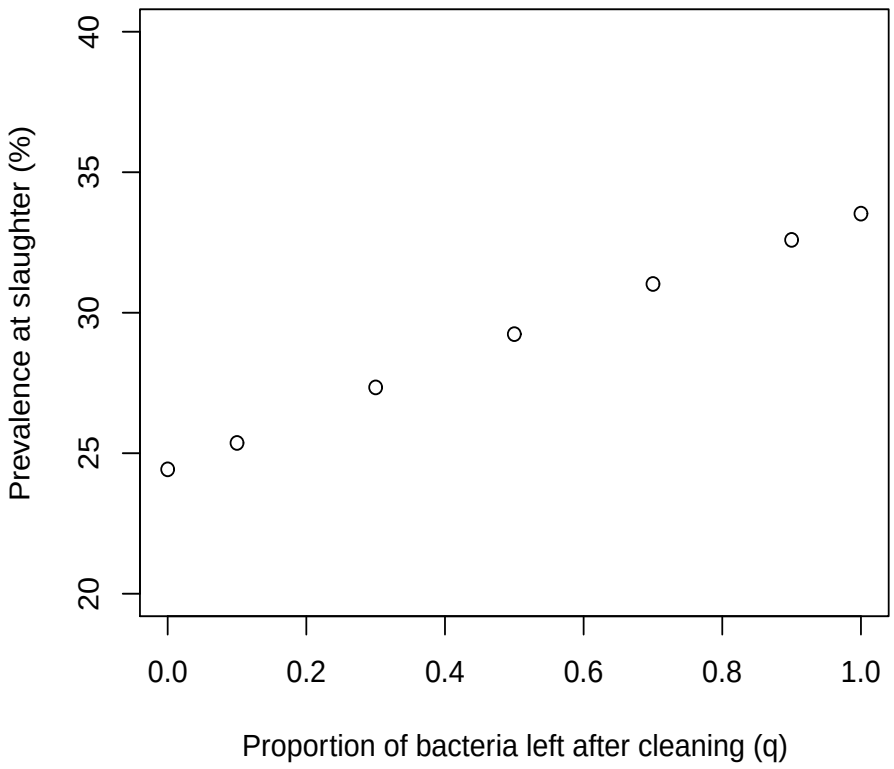

Figure 8.1: Mean *Salmonella* prevalence with varying levels of efficiency of cleaning and disinfection

8.3 Probability of infection after *Salmonella* exposure

As stated previously, a mode of action for *Salmonella* intervention is to reduce the probability of becoming infected after exposure to *Salmonella*. A 10 times reduction in p caused the prevalence to decrease from $\approx 25.4\%$ to $\approx 7.29\%$. Conversely, a 10 times increase resulted in a prevalence of approximately 90.82% (Figure 8.3), which was a similar result to that obtained within the slatted models (Chapter 6). As such, it appeared as though, with these levels of shedding, the probability of infection had much the same impact on

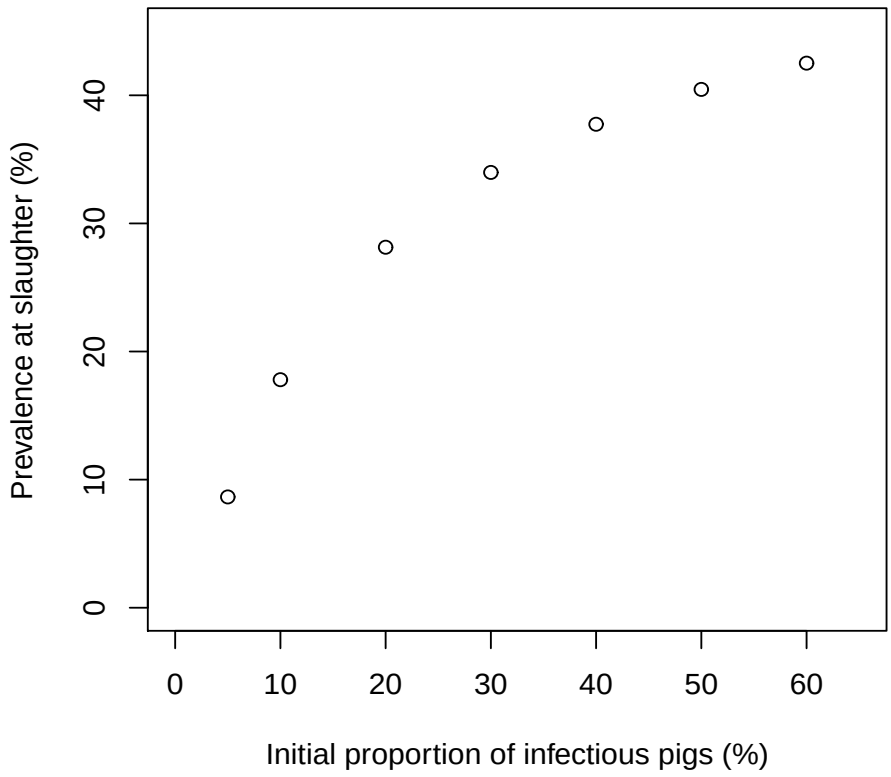

Figure 8.2: Mean prevalence level prior to slaughter with varying numbers of initial infectious pigs entering the solid-floored unit

Salmonella prevalence at slaughter regardless of the structure of the unit itself.

8.4 Rate of reversion to infectiousness

Although the majority of stress that could cause a pig to resume shedding would occur during transport and lairage, analysis of the effect of stress on the animals can be implemented nevertheless. Tasks such as the movement of animals has been shown to increase

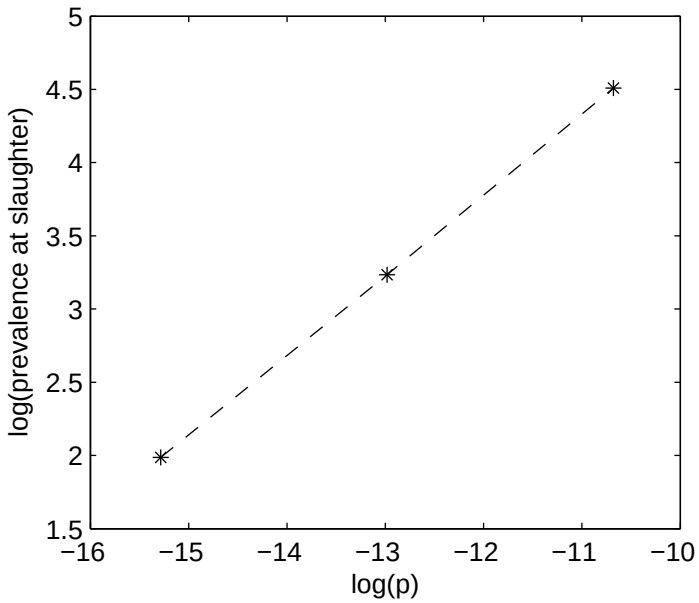

Figure 8.3: Graph highlighting the effect of the probability of infection(p) on *Salmonella* prevalence in slaughter age pigs. Natural logs were used, with base parameter $log(p) = -12.98$.

the amount of stress imposed on them (Lo Fo Wong et al. [2002]). The model showed that the average on-farm prevalence increased as the rate of resuming shedding became greater (Figure 8.4). However, what was interesting was the fact that animals frequently resuming shedding ("frequent reversion") consistently appeared to only take effect after approximately 20 days, before which animals occasionally and frequently resuming shedding ("occasional" and "frequent reversion") showed similar behaviour. This was typical of most simulated trajectories, however it was not clear why the divergence appears at approximately 20 days. One possible reason for this observed shift, is that after approximately 3 weeks, the effects of cleaning become inadequate due to the increased number of animals shedding. At this point, because of the potentially large numbers of bacteria in the environment, the rate at which animals become infectious increases drastically as the

cleaning is unable to remove sufficient numbers of bacteria before an infection occurs.

Within both the solid and slatted units (Figures 8.4 and 6.3) animals infrequently and occasionally resuming shedding (infrequent and occasional reversion) showed a similar pattern. However, within the solid unit, the prevalence at slaughter for animals frequently resuming shedding was higher than that within the slatted counterpart.

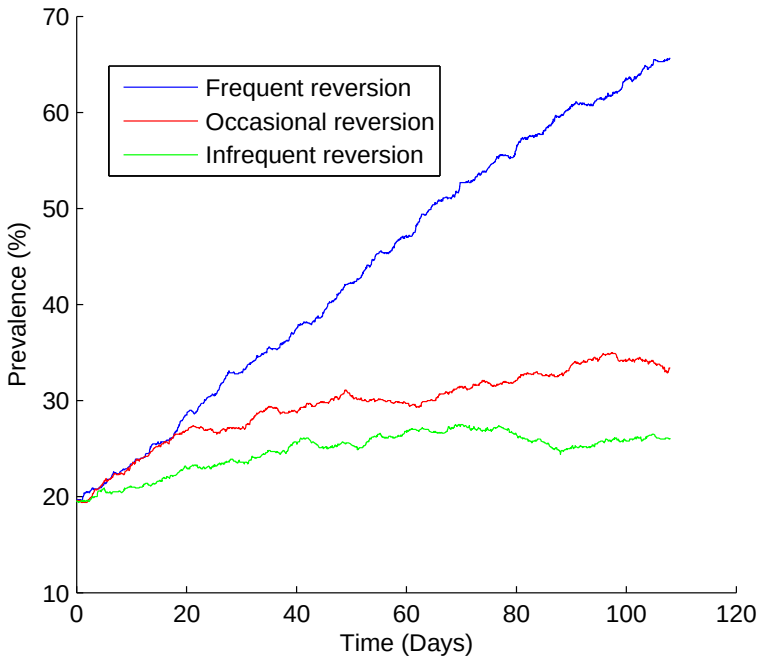

Figure 8.4: Effect of the rate of reversion to infectiousness (δ) on *Salmonella* prevalence. Note: $\delta = \frac{1}{14}$ for frequent reversion, $\delta = \frac{1}{61}$ for occasional reversion and $\delta = \frac{1}{108}$ for infrequent reversion.

It is possible that animals frequently resuming shedding crosses a threshold which resulted in the continued increase of prevalence. By differentiating the *Salmonella* status of the animals frequently resuming shedding, it was shown that the average number of

both infectious and carrying animals continually increase (Figure 8.5). When animals frequently resume shedding, there is in an increase in the number of animals capable of passing on infection, which consequently results in an increase in *Salmonella* prevalence.

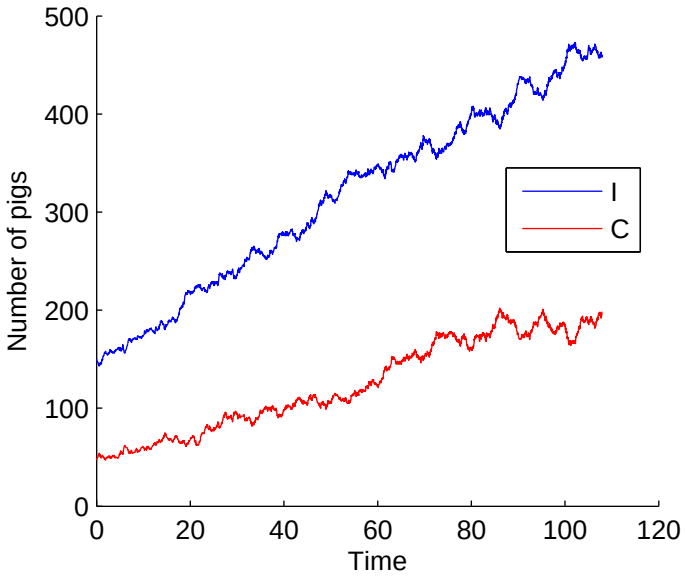

Figure 8.5: Differentiation between infection status with frequent reversion $\left(\delta = \frac{1}{14}\right)$

8.5 Duration of excreting and carrying the bacteria

A major advantage with producing models, is that individual aspects of the system can be analysed to assess the extent to which they can affect the outcome; *Salmonella* prevalence in this case. Although a decrease in the duration of shedding or carrying the bacteria affected the prevalence prior to slaughter (Figure 8.6), the results were very small for potentially a large amount of effort. Similar results were found within the slatted unit (Figure 6.5).

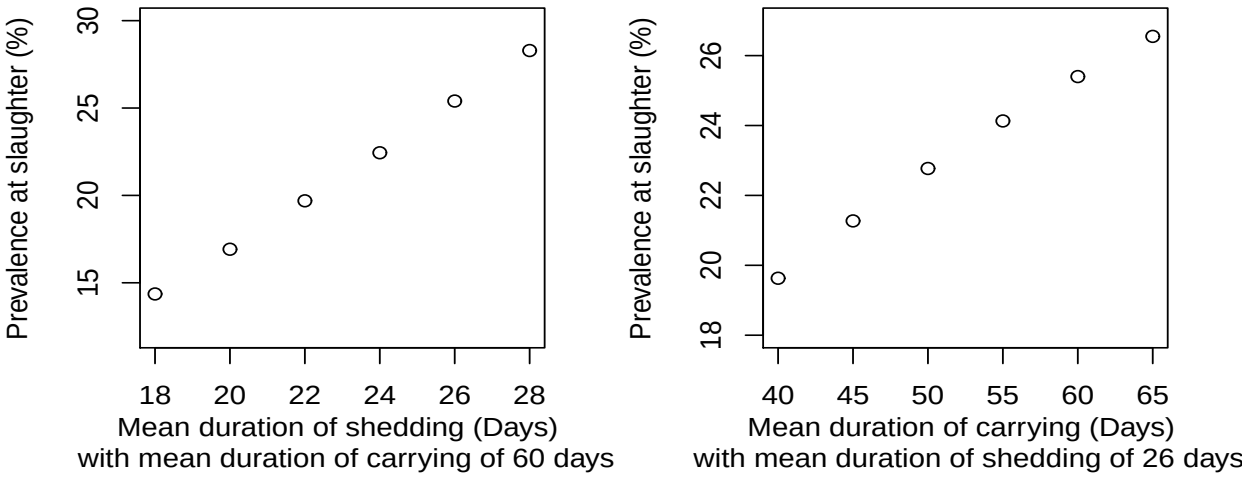

Figure 8.6: Mean prevalence level with varying durations of excreting and carrying *Salmonella*

8.6 The effect of shedding on herd prevalence

It has already been shown that high shedding on farm could cause a large outbreak in *Salmonella* infection (Chapter 6). Within the solid-floored unit, a 10 times higher rate of shedding resulted in the average prevalence prior to slaughter to increase from 25.4% to $\approx$ 90.85% (Figure 8.7), which showed similar results with the slatted unit (Figure 6.7).

This prevalence was similar to the corresponding prevalence within the slatted flooring, which potentially highlights that the on farm prevalence was not dependant on the building structure when shedding was at high levels. The main difference between farm structure was highlighted when looking at the introduction of 1 infectious animal. It was shown that within the slatted unit (Figure 6.9) infection took a long time to become established (approximately 60 days). Within the solid unit however, the dynamics were

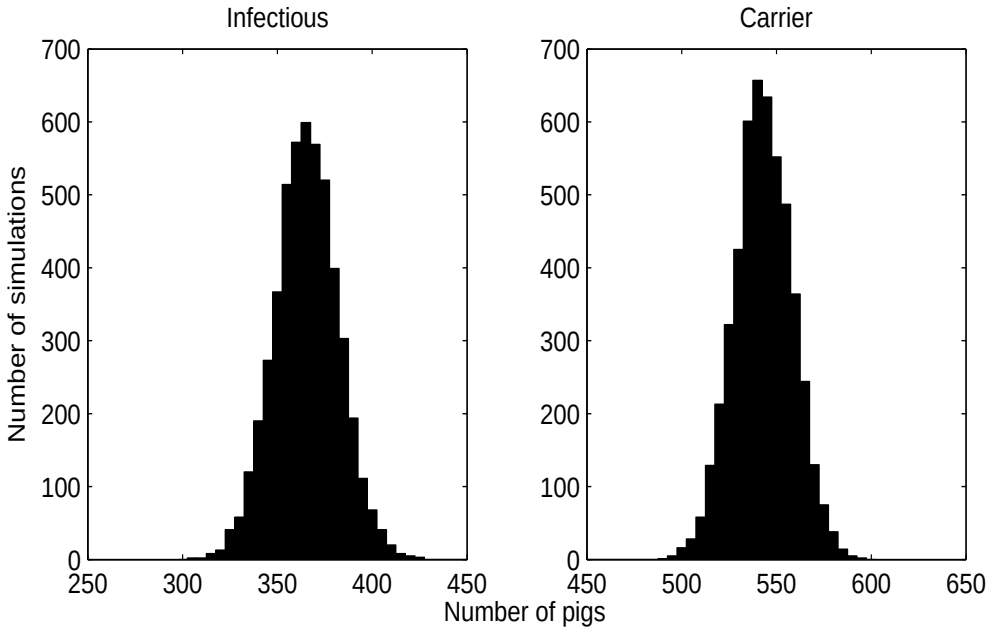

Figure 8.7: The effect of a 10-fold increase in shedding on *Salmonella* prevalence on a 100-place, solid-floored unit. Histogram shows the distribution of the numbers of infectious and carrying pigs at the end of the finishing stage of production

extremely different, with infection becoming established within 15 days (Figure 8.8). Furthermore, the prevalence prior to slaughter differed considerably between farm types with the introduction of 1 infectious animal: the slatted unit had a prevalence of approximately 58%, whereas the solid unit had a prevalence of approximately 92%. As all bacteria shed were available for consumption within the solid unit, it was thought that this enabled a quicker uptake of infection, which consequently resulted in a greater slaughter age prevalence. As such, it was thought flooring type played a major role within this scenario.

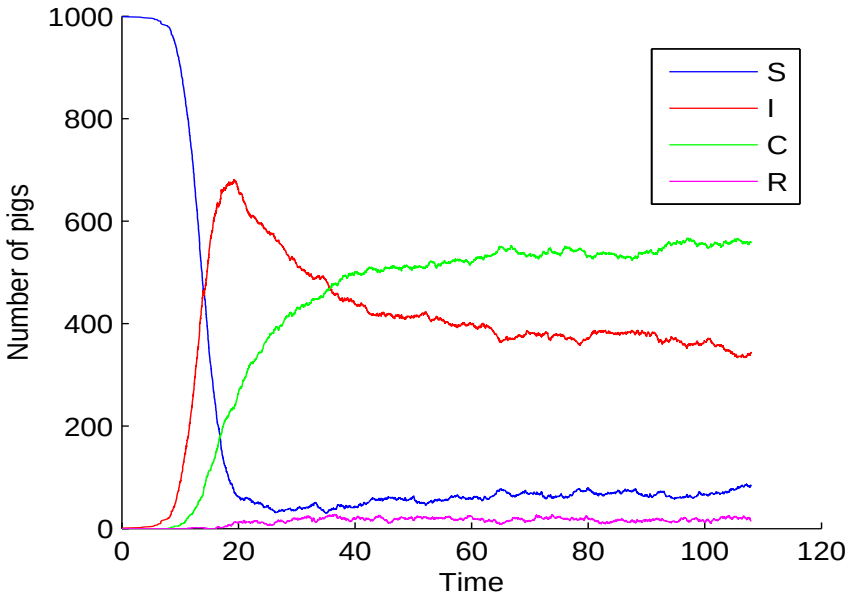

Figure 8.8: A plot of a trajectory when one infectious pig, shedding high levels of *Salmonella* ($\lambda = 2.25 \times 10^5$) is introduced into a fully susceptible population

8.6.1 Interventions affecting *Salmonella* prevalence with the presence of a number of "super-shedding" pigs

In order to fully understand how effective cleaning and disinfection can be on *Salmonella* control, the model was simulated with various levels of efficiency when shedding was high. It was shown (Figure 8.9) that when shedding was high, cleaning was not as effective in controlling *Salmonella* prevalence on farm. In fact, the difference in the average *Salmonella* prevalence between farms with a high level of cleaning and those with a low level of cleaning was less than 1%. What this potentially indicates is that infection can become established extremely quickly and consequently the cleaning of the farm is rendered inadequate. As such, it is quite possible that in order to control *Salmonella* spread when shedding is high, cleaning must be conducted more often in order to minimise the amount of bacteria that pigs are exposed to.

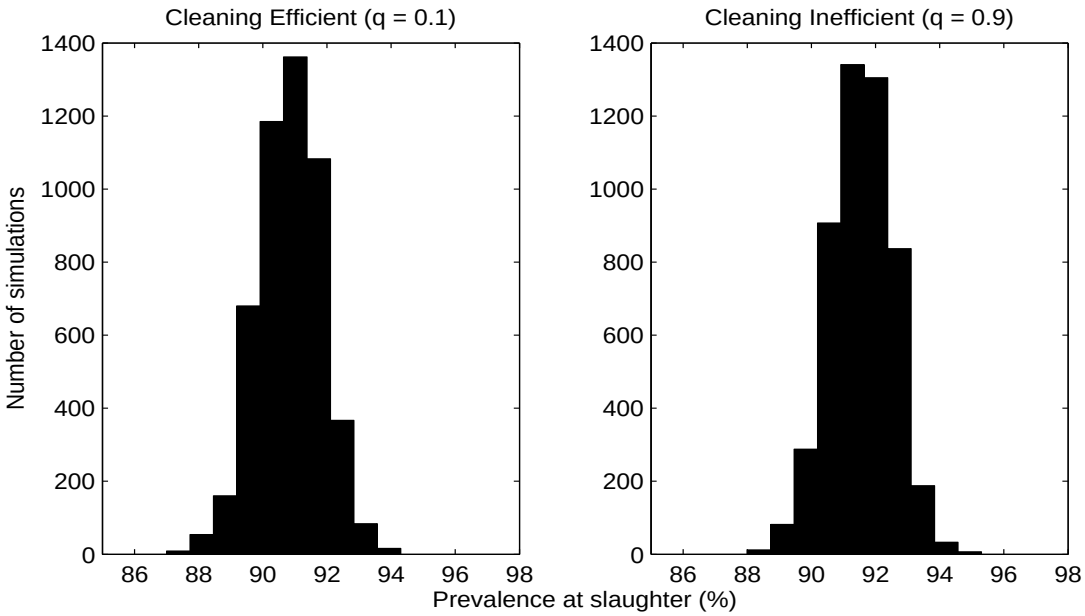

Figure 8.9: *Salmonella* prevalence with varying efficiencies of cleaning and disinfection. A histogram showing the distribution of *Salmonella* prevalence with a good and poor standard of cleaning and disinfection on farm

Within both models, the probability of becoming infected after *Salmonella* exposure was shown to be a key driver of *Salmonella* transmission. With a high rate of shedding, a 10 times reduction in probability found prevalence fall to 25.44%; a reduction of $\approx 65\%$. A plot of 1 typical trajectory representing the prevalence, showed the number of infectious and carrying pigs to fluctuate (possibly around an equilibrium point) but certainly without showing signs of falling drastically within the permitted time (Figure 8.10). As such, an intervention that targets the probability of infection could be highly influential in reducing *Salmonella* prevalence at slaughter.

Although a reduction in the initial prevalence alone would not be guaranteed to have

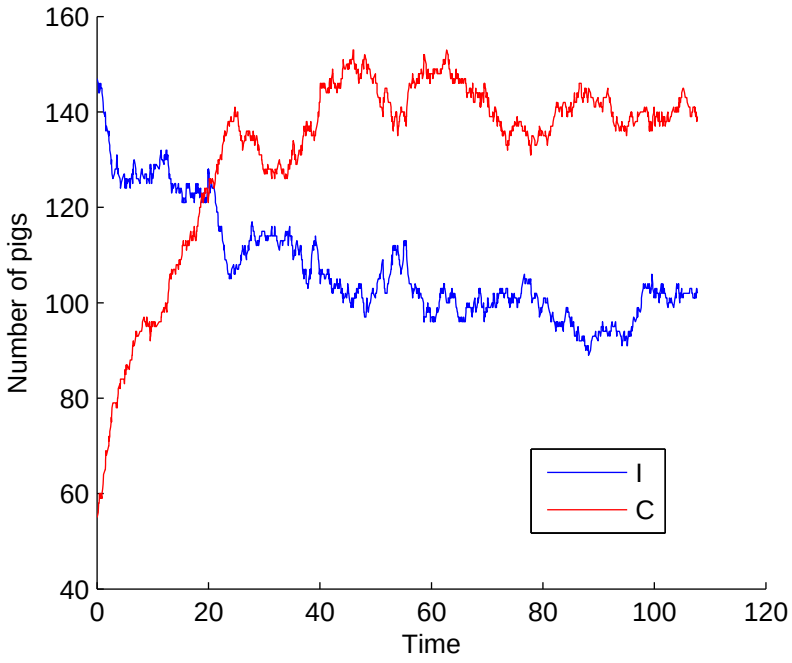

Figure 8.10: A plot of a trajectory showing the effect of a reduction in the probability of infection on the number of infectious and carrying animals ($\lambda = 2.25 \times 10^5, p = 2.3 \times 10^{-7}$)

a large effect in *Salmonella* control (both with high and "normal" shedding levels), due to the fact the model does not account for anomalies and other influences, when combined with another intervention that targets *Salmonella* dynamics in a more direct way, the result could be extremely beneficial. This highlights that some form of control measures in place throughout the life cycle of a pig could result in reducing the *Salmonella* burden. For example, as little as 1% of infectious animals, shedding high numbers of bacteria still resulted in a prevalence in the region of 90%. This is clearly unsurprising as the introduction of 1 infectious animal was sufficient to cause an outbreak (Figure 8.8). However, a reduction in the initial proportion of infected animals entering the unit in conjunction with a reduction in the probability of infection could result in a high level of *Salmonella* control.

It was shown that animals frequently resuming shedding could result in an increase in prevalence. However, when shedding was high, the rate at which animals resume shedding had a much lower effect on average *Salmonella* prevalence prior to slaughter (Figure 8.11). All rates lead to similar behaviour for the first 14 days, after which animals that frequently resume shedding resulted in a slightly higher prevalence, but all trajectories appear to settle to equilibrium. This was a similar result to the slatted floored unit (Figure 6.12). The main difference was the dynamics, whereby infection was more gradual within the slatted unit, compared to the quick initial rise in prevalence within the solid unit.

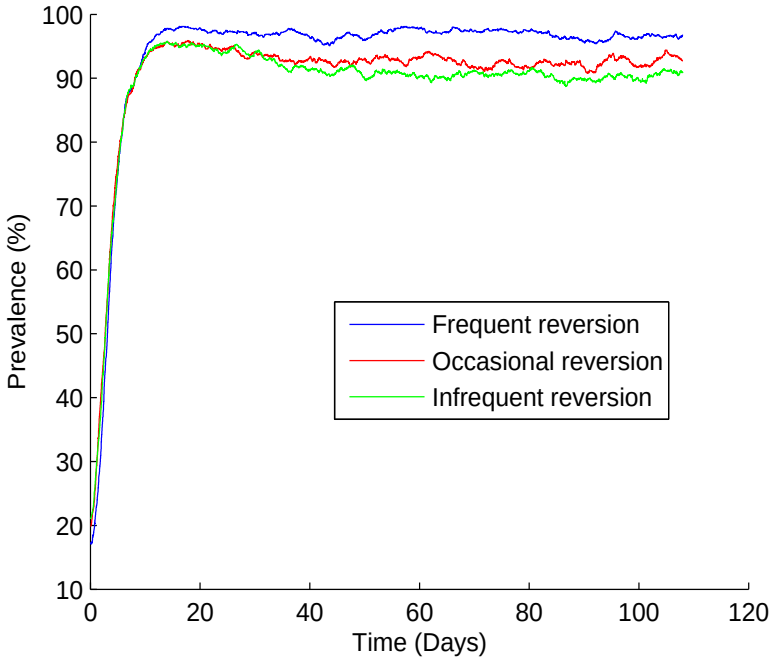

Figure 8.11: The effect of the rate of reversion to infectiousness on *Salmonella* prevalence when shedding was high ($\lambda = 2.25 \times 10^5$). Note: $\delta = \frac{1}{14}$ for frequent reversion, $\delta = \frac{1}{61}$ for occasional reversion and $\delta = \frac{1}{108}$ for infrequent reversion.

What was interesting was the extremely small difference in prevalence with these

varying rates at which an animal resumes shedding; a difference of approximately 6%. This is clearly a considerable difference compared to "normal" shedding levels, where frequently resuming shedding resulted in a prevalence of approximately 40% higher than infrequently resuming shedding (Figure 8.4). The prevalence of *Salmonella* consists of a number of animals carrying the bacteria and a number of animals shedding the bacteria. When shedding was high, the majority of the population was already infected in some form, and as such, frequently changing between states does not have such a large effect. However, with "normal" shedding levels, frequent transition between carrying and shedding (and therefore infectious) states can have a drastic affect, as there are a larger number of animals that are capable of passing on the infection.

8.7 Discussion

This chapter investigated interventions implemented on the solid-floored unit described in Chapter 7 in an attempt to highlight possible modes of action that result in a decrease in *Salmonella* prevalence.

The model highlighted some key findings with regard to cleaning and disinfection on farm. The results from the model were in accordance with the results from an on farm trial, whereby improved cleaning resulted in a decrease in prevalence of approximately 8% (Armstrong [2010]). Furthermore, this added to the evidence found in Chapter 2 that cleaning and disinfection alone is insufficient in fully controlling *Salmonella*. Interestingly, when the number of bacteria shed was high, cleaning had a minimal effect on *Salmonella* prevalence, which was likely to be due to the rate at which infection was able to spread. In an attempt to counteract this high rate of spread with the use of cleaning, it is pos-

sible that frequent cleaning of the unit could minimise *Salmonella* spread. Although this has not been modelled here, the fact that cleaning does have some effect on reducing the prevalence was thought to confirm this supposition. However, the cost in terms of time and monetary value would need to be explored in order to determine whether this would be feasible, beneficial and economically viable.

The amount of bacteria shed after infection and the probability of infection were found to be important aspects and key drivers in *Salmonella* transmission on farm at all levels of shedding, which is similar to the findings within Chapter 6. It was shown that infection could spread incredibly quickly throughout the unit when shedding was high (with a peak in infectious animals after approximately 10 days) due to an increased availability of bacteria within the environment. Although there was not much of an implication with regard to *Salmonella* prevalence at slaughter weight, as both units show a similar prevalence (Figure 9.1), there are nevertheless implications with regard to the application of an intervention. With the accelerated uptake of *Salmonella* infection, the time at which an intervention should be applied in order to be as effective as possible may need to be during the initial uptake of infection. However this would require further investigation. A number of empirical studies have shown that rapid transmission is possible when animals are infected with a high dose of *Salmonella* (Wood et al. [1989], Osterberg and Wallgren [2008]). As the amount of bacteria that an animal is exposed to was high, it is not unreasonable for the model to exhibit a similar behaviour. Consequently, the results obtained from the model were not thought to be implausible.

Chapter 9

Discussion

Besides developing models of *Salmonella* transmission, this PhD involved close collaboration with the industry. The trial of the BPEX ZNCPig *Salmonella* farm risk assessment tool as part of this CASE studentship placement highlighted some important findings for the industry and provided an invaluable insight and experience in the industry. The results from the tool also provided additional evidence used within the models. The finding that Platinum farms were likely to adopt a subset, rather than all biosecurity practices should encourage farms to adopt a range of biosecurity practices rather than focusing on 1 aspect of biosecurity. With a small number of modifications to the Farm Tool Questionnaire, a well constructed database with a copious amount of data could be generated for the industry to analyse. Due to the pilot nature of this study, and the small sample size, it may be best to view this study as hypothesis generating, rather than hypothesis testing. In this light, the study suggests a number of hypotheses worthy of further investigation. The use of a detergent and ensuring transport is visibly clean before loading were found to significantly reduce culture prevalence (p-values 0.03 and 0.05, respectively). Good staff hygiene, efficient management of sick pigs and a good standard of cleaning and disinfection were qualities identified that resulted in a good *Salmonella* score.

Three stochastic models describing *Salmonella* transmission within varying farm structures were developed: A single-roomed, fully-slatted floored SICRS/W model, a multiple-roomed, fully-slatted floored SICRS/W model and a single-roomed solid floored SICRS/W model. The aim of this thesis was to develop models of *Salmonella* transmission within a pig herd and use these models to investigate where control strategies should be aimed. Furthermore, the results obtained from the study help improve the understanding of *Salmonella* dynamics on UK pig farms and add to the evidence base available to the industry for decision making.

The models identified some key results with regard to on-farm *Salmonella* dynamics. The number of bacteria shed and the probability of infection after *Salmonella* exposure were found to be key drivers of *Salmonella* transmission. What was highlighted was the importance of the environmental pool on the ability for transmission. The models also highlighted the potential inadequacy of cleaning and disinfection, notably so when bacterial shedding was high. What could be of potential importance would be the time interval at which cleaning and disinfection were carried out. These results should help the industry by highlighting key areas where interventions should be applied, in order to gain effective *Salmonella* control. However, a principal finding showed that there is not a single key action that can solve the problem, but rather, because of the complexity of the system, a number of aspects should be targeted.

Each model enables the assessment of different aspects of *Salmonella* dynamics. The model for the slatted style unit allows the calculation and analysis of the basic reproduction number, that has never previously been analysed for this type of system. It was

shown that the basic reproduction number R_0 was insufficient in determining whether the disease was eliminated or persists, due to the complex dynamics. It was shown that when $R_0 < 1$, the disease does not necessarily disappear (over the relevant time period) when a certain number of infectious animals were introduced into the population. As such, R_0 calculations may not be the most effective way of examining interventions applied within this system when shedding levels are "normal", due to the complex dynamics. The solid style unit on the other hand takes into account the effect that cleaning and disinfection has on the dynamics. As cleaning and disinfection was implemented, R_0 calculation for the solid floored system was not implemented as the calculations would be too complicated in order to account for this effect.

The initial prevalence of *Salmonella* entering the unit had some effect with ordinary shedding levels within both the slatted and solid models. This could indicate that lowering the prevalence in the breeding unit could directly result in a low *Salmonella* prevalence at slaughter. However, simply lowering the prevalence in the breeding unit is unlikely to ensure prevalence remains low at slaughter weight, and can not be deduced from these models, as the models fail to account for alternative sources of infection and the involvement of fomites in the route of *Salmonella* transmission. A major difference between the 2 models however was shown with the introduction of 1 infectious animal when shedding was high; the speed in which infection spreads within a solid unit was considerably quicker compared to the slatted counterpart. Interestingly, we saw minimal difference in prevalence prior to slaughter between the models, which indicated that although *Salmonella*, if present in high doses, could spread more quickly within a solid unit, the final number of animals infected was similar. However, the dynamics between the models were

very different, as shown in Figure 9.1. The difference in dynamics was potentially due to a dampened uptake of infection with the presence of the slatted floor, due to the lower amount of available bacteria. Within the solid unit, animals are immediately exposed to a larger amount of bacteria and it is therefore not unreasonable that the uptake of infection is faster within this style of unit. Although the model showed rapid transmission, studies that infect animals with a high dose of *Salmonella* show there is a potential for this rapid transmission (Wood et al. [1989], Osterberg and Wallgren [2008]). As such, the results obtained from the model were not thought to be implausible.

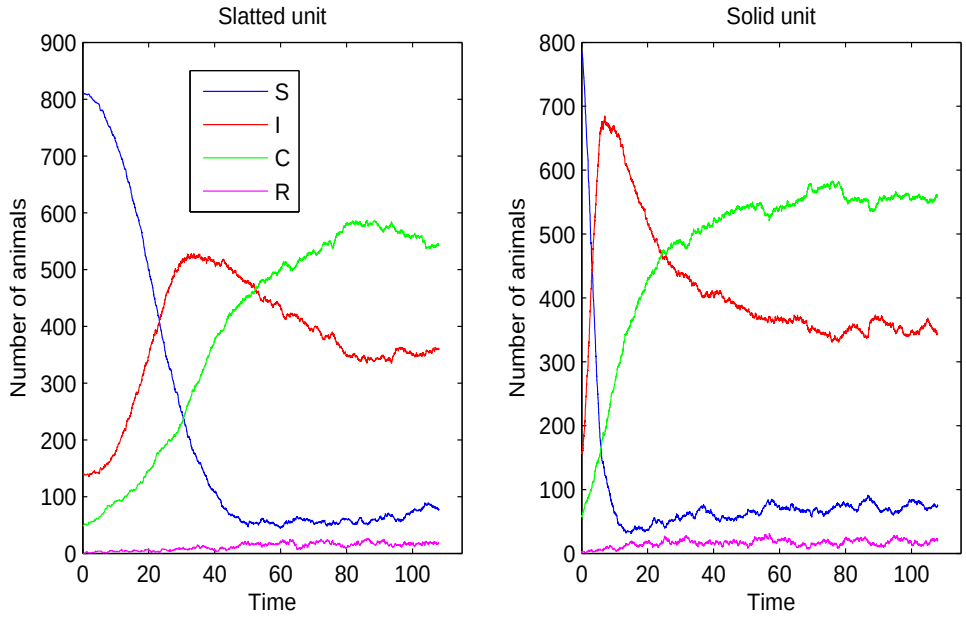

Figure 9.1: A plot of one trajectory for each model showing the prevalence for each class with a high shedding rate

One parameter that had a profound affect on *Salmonella* prevalence was the probability of becoming infected after *Salmonella* exposure. As such, interventions aimed at this parameter should produce noticeable results. Within all models, the probability of

infection was seen to be one of the key drivers of *Salmonella* transmission, and any interventions imposed on farm that could reduce the probability of infection would be beneficial to the industry. However these interventions would have to be cost effective in order to be fully beneficial and economically viable. There are a number of factors that could influence the probability of becoming infected. Studies have shown that a typical infectious dose is 10^6 cfu (Gray et al. [1996b], Osterberg et al. [2009], Osterberg and Wallgren [2008]). As vaccines aim to limit the chance of infection and prevent the colonization of the host (Potter et al. [2008], Rostagno [2011]), it is possible that vaccination could result in the infectious dose increasing to a value that is beyond the amount of bacteria present; therefore resulting in a decrease in the probability of infection.

The models highlighted the potential damaging effects of a high rate of shedding on farms in increasing farm prevalence. Although the models did not explicitly model "super-shedders," it could be argued that farms with a high *Salmonella* prevalence are likely to have a number of pigs shedding large numbers of bacteria, "super-shedding" pigs. Studies have shown a wide array of *Salmonella* numbers shed in pigs (Gray et al. [1995, 1996a], Smith and Jones [1967], Gutzmann et al. [1976]) and the existence of super shedders in other species has been proved (Matthews et al. [2006], Arthur et al. [2010]). Although this study does not prove the existence of "super shedders," it is thought that these other studies do indicate the presence of such animals. What, however, this study does show is the potentially damaging effects the presence of these animals can have on *Salmonella* prevalence in slaughter age pigs. The result from the models highlighted the need for further research on why some pigs shed such high levels of *Salmonella* and how the amount shed could be minimised. It would be interesting to see whether vaccination had this effect at

a population level and whether "super-shedders" can be eliminated by vaccination. If the reason for increased shedding is related to an impaired immune response to *Salmonella*, then it is possible that "super-shedders" may not respond to vaccination. The models do show however, that containing these infected animals was the best attempt to control the number of animals that are exposed to these highly infectious individuals.

Arguably the presence of a recovered state within the models is unnecessary due to the amount of time spent within the infectious and carrier class. However, as such a state was thought to exist, its inclusion was for completeness. Furthermore, the state could be used in order to analyse the effect of a vaccination as it could be assumed that vaccination decreases the susceptibility of the animals by inducing a temporary immunity to *Salmonella* infection.

As always with mathematical modelling, a complex and time consuming task was gathering the evidence for estimating the parameter values used within the models. Although secondary data were used to estimate the parameters, which is clearly not ideal, collecting additional, new data needed was simply out of the scope of this study. However the best possible estimates for realistic parameter values were used.

9.1 Future work

There are a number of extensions that could be made to the models in the future. The models could be extended to include other aspects of production, transport to the abattoir for example. The models that have been developed were set up in order to make certain extensions, such as abattoir transport, feasible.

Within the models presented, the transmission of *Salmonella* was analysed rather than its introduction. As such, a further extension to the models could be to incorporate and analyse how infection is initiated and established on farm. The models go some way in explaining how infection can be established on farm. However, the initiation of *Salmonella* could be incorporated by analysing rodent and bird effects or via contaminated feed/feed trucks for example, both of which have been shown to have an effect (Meerburg and Kijlstra [2007], Harris et al. [1997], Fedorka-Cray et al. [1997]). Although the effect of rodents and birds could be allowed for here, by incorporating their presence as an aspect of environmental bacteria for example, it was thought that the effect would be minimal once infection was established. Therefore, rather than looking at the presence of alternative sources of infection when infection is present, it may be more beneficial to observe these sources as an instigator. It is however possible that rodents and other fomites have an effect in spreading infection between groups of animals in separate rooms. Consequently, further investigation is required to measure the extent to which rodents affect the dynamics.

Although there are a number of extensions and modifications that could be applied to the current models, it is still thought that the results obtained give some useful and important information for the industry. Simulations of the models identified where control strategies should be aimed to result in some form of *Salmonella* control on farm. Interventions that target the probability of infection after *Salmonella* exposure and the amount of bacteria shed once an animal becomes infectious should have the biggest effect on *Salmonella* prevalence. Furthermore, the results identified other areas of research for the industry to explore, and that could further add to the evidence base available to the pig

industry, in an attempt to have a high level of *Salmonella* control.

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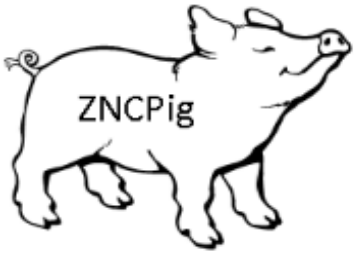
Appendix A

BPEX ZNCPig *Salmonella* Farm Risk Assessment Tool

Reproduction of this questionnaire has reduced the clarity, however it should only be used as a point of reference for Chapter 2.

ZNCPig Salmonella Farm Risk Assessment Tool



FARM ID: _____

VISIT DATE: _____

Name of vet: _____

ZNCPig SALMONELLA FARM TOOL

Owners Name:	
Managers Name:	
Farm Address:	
County:	
Postcode:	
Telephone:	
Farm assurance:	ABP/Genesis/QMSFA/None - Number ☐☐☐☐☐☐
CPH Number(s):	
Marketing group:	

Does this farm have a Salmonella Control Plan?	Yes ☐	No ☐
Does this farm have a Farm Health Plan?	Yes ☐	No ☐
Is this farm a member of BPHS or Wholesome Pigs Scotland?	Yes ☐	No ☐
Is the farm involved in a regional health improvement programme?	Yes ☐	No ☐
Are all pigs on this farm kept on one site?	Yes ☐	No ☐
Do pigs move between sites that are under the same management?	Yes ☐	No ☐

1

ZNCPig Salmonella Farm Risk Assessment Tool

BPEX and the Food Standards Agency are developing a tool to assess the control of risk factors for Salmonella carriage in pigs on pig farms.

The aim is to use established principles to develop the background information and propose audit style questions indexed to the scientific evidence with proposed relative scoring for pig farms for the control of Salmonella on pig farms.

The tool will link together the outputs from relevant international research projects and available published scientific evidence on Salmonella in pigs with objective information on their implementation that could be obtained on pig farms. It should be possible to use the tool developed to assess how well a farm is controlling risk factors associated with Salmonella carriage by pigs and to identify areas where changes to improve the control of Salmonella could be made.

Thank you for agreeing to participate in the testing of the draft ZNCP Salmonella farm risk assessment tool. Please complete the questionnaire which follows as accurately as possible.

Please enter information on what is actually being done on the farm currently and not what it is intended to do or what was planned to be done.

As far as possible the questions should be answered on the basis of what has been done over the past 4 weeks or for the most recent group of pigs managed for areas of the farm that have been destocked.

2

ZNCPig SALMONELLA FARM TOOL

Section 1 - PIG UNIT TYPE AND LOCATION

1.1	How far away is your nearest pig farm?	Less than 10km ☐		No known pig units within 10km ☐	

Section 2 - HEALTH BACKGROUND

2.1 Health background: Evidence of disease, by site/stage

2.1.1. Evidence of disease

2.1.1.1.	Is there any evidence of respiratory disease (pneumonia, coughing etc.) on farm?	Yes ☐	No ☐
2.1.1.2.	Is there any evidence of enteric disease (scouring, ileitis, dysentery etc.) on farm?	Yes ☐	No ☐

If yes, what are the main causes of enteric disease on farm? _____

2.1.1.3.	Is there any evidence of wasting disease (PMWS, PDNS, PCVD) on farm?	Yes ☐	No ☐
2.1.1.4.	Is there any evidence of parasitic disease (Ascarid, milk spot liver, mange) on farm?	Yes ☐	No ☐

2.1.2. Vaccination policy

2.1.2.1.	Do you use a vaccine for PMWS/PCVD for any pigs on the farm?	Yes ☐	No ☐

If yes, which vaccine do you use? _____

2.1.2.2.	Do you use a vaccine for Enzootic Pneumonia for any pigs on the farm?	Yes ☐	No ☐

If yes, which vaccine do you use? _____

2.1.2.3.	Do you use a vaccine for PRRS for any pigs on the farm?	Yes ☐	No ☐

If yes, which vaccine do you use? _____

2.1.2.4.	Do you use a vaccine for ileitis for any pigs on the farm?	Yes ☐	No ☐

Section 2 - HEALTH BACKGROUND

Supporting evidence requirement:

Farm health plan documentation backed by vet script/invoices for vaccine

2.2 Salmonella vaccination

2.2.1. Do you use a vaccine for Salmonella for any pigs on the farm?	Sows ☐	Pigs less than 6 weeks of age ☐	Pigs over 6 weeks of age ☐

If yes, which vaccine do you use? _____

2.2.2. Salmonella vaccination policy

2.2.2.1.	Vaccination of progeny: Use of live Salmonella vaccine	Yes ☐	No ☐
2.2.2.2.	Vaccination of sows: Use of live Salmonella vaccine	Yes ☐	No ☐
2.2.2.3.	Vaccination of progeny: Use of live Salmonella poultry vaccine orally administered off license under direction of vet	Yes ☐	No ☐
2.2.2.4.	Vaccination of sows: Use of emergency (autogenous) Salmonella vaccine which may be used under special VMD license under direction of vet	Yes ☐	No ☐

Supporting evidence requirement:

Farm health plan documentation backed by vet script/invoices for vaccine

4

Section 3 - INCOMING STOCK

Incoming stock represents a significant risk to the pigs on your unit due to the risk of *Salmonella* transmission between pigs. This will include both replacement gilts and boars on a breeding unit and weaners on a growing site.

3.1 Incoming Stock: Number of sources

3.1.1. From how many different sites or holdings have pigs come from within the last 6 months?

DON'T KNOW	☐
NONE i.e. closed herd so no risk through incoming pigs	☐
1 site/holding only	☐
1-3 different sites/holdings	☐
More than 3 sites/holdings	☐

Supporting evidence requirement:

Movement record documentation
Movement data (electronic data hub of AML2 and FCI records for England and Wales due to be operational by April 2011)

3.2 Incoming Stock: Salmonella Status of incoming pigs

3.2.1. Do you know the Salmonella status of your incoming pigs?

Do not know – have not asked	☐
Asked, but supplier did not know or confirmed to be Salmonella positive	☐
Confirmed to be Salmonella free and can provide credible evidence to back this up (see Supporting Information)	☐

Supporting evidence requirement:

Link to what is deemed acceptable eg no. of samples, over what time period, bacteriology v serology?

5

Section 4 - GENERAL BIOSECURITY

BIOSECURITY

On it's own, biosecurity is not a control measure but a pre-requisite for other measures. Whilst a biosecurity plan might not have hard evidence for effectiveness in Salmonella control as individual control measures but collectively external and internal biosecurity measures, designed to minimise the risk of disease entering the farm and spreading within the farm as well as between farms, is considered helpful in lowering background environmental infection levels.

There are many routes by which Salmonella can be introduced onto a farm and the organism is often disseminated widely on farms. Control measures include changes of clothing and boots for visitors, bird and rodent control, foot-baths containing active disinfectant outside houses, limiting access to the site by visitors and lorries, etc. Farm size, stocking densities and pig density within a region all have a negative effect on the Salmonella status of a farm, perhaps by predisposing to Salmonella spread within and between farms via lax biosecurity.

4.1 Management practice: biosecurity

4.1.1. Have you carried out a biosecurity audit of your farm in the last three months? Yes ☐ No ☐

4.2 If, yes, how did you score?

Top 25% ☐

Mid 50% ☐

Lower 25% ☐

OPPORTUNITY TO INPUT SCORE FROM BPEX BIOSECURITY SCORING TOOL AT THIS STAGE

OR

COMPLETE SECTION 4.3

4.3 How many of the following 7 key elements of external and internal biosecurity practice outlined below are included in your unit biosecurity plan where you met the criteria specified throughout the last 4 weeks?	**/7**

4.3.1. Do you use foot dips effectively over the last 4 weeks – ie do you fulfil at least 6 of the following 9 requirements? **/9**

4.3.1.1. Supply a footdip containing an approved disinfectant at its maximum recommended concentration (see link to disinfectants approved list) and supply a boot brush *at the entry to every building* and *at every entrance to the pig unit*? Yes ☐ No ☐

4.3.1.2. Provide footdips large enough to hold at least one large boot and contain enough disinfectant to cover the whole foot to over the ankle when immersed for a minimum time period of 20 seconds? Yes ☐ No ☐

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Section 4 -	GENERAL BIOSECURITY		
4.3.1.3.	Ensure that the disinfectant chosen is approved for use in footdips and are aware of the required strength	Yes ☐	No ☐
4.3.1.4.	Provide footdips in covered areas to prevent them from being diluted by heavy rain and replace dip immediately it has become diluted?	Yes ☐	No ☐
4.3.1.5.	Supply brush with each footdip to remove visible muck from boots every time staff enter and leave the site, and every time that staff enter and leave a building?	Yes ☐	No ☐
4.3.1.6.	Empty and replenish footdips when visibly soiled, **at least once every week or more often once they become soiled**?	Yes ☐	No ☐
4.3.1.7.	Require separate boot washing to be undertaken by all staff, especially on muddy sites, before dipping boots in disinfectant?	Yes ☐	No ☐
4.3.1.8.	Test footdip contents using indicator strips to confirm presence/absence of active ingredient	Yes ☐	No ☐
4.3.1.9.	Require all staff and visitors to use footdips and boot brushes?	Yes ☐	No ☐
4.3.2.	**Do you manage the biosecurity risk from visitors effectively over the last 4 weeks – i.e. do you fulfil all 3 of the following requirements?**		**/3**
4.3.2.1.	Insist on only essential visitors visiting the unit?	Yes ☐	No ☐
4.3.2.2.	Insist that essential visitors wear clean boots and protective clothes provided by the unit, washed and disinfected after use?	Yes ☐	No ☐
4.3.2.3.	Insist on visitors not entering any building or pen containing pigs unless essential for the purposes of the visit?	Yes ☐	No ☐
4.3.3.	**Do you manage the biosecurity risk from staff effectively in the last 4 weeks – i.e. you fulfil at least 4 out of the following 5 requirements**		**/5**
4.3.3.1.	Ensure all farm staff are provided with farm overalls and boots?	Yes ☐	No ☐
4.3.3.2.	Provide staff with proper changing and washing facilities?	Yes ☐	No ☐
4.3.3.3.	Provide lavatory facilities with adequate handwashing facilities at least at a single central point on the unit with separate discharge to septic tank?	Yes ☐	No ☐
4.3.3.4.	Insist on farm staff not having contact with other pigs?	Yes ☐	No ☐
4.3.3.5.	Do not allow the sharing of staff and equipment with other units?	Yes ☐	No ☐

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Section 4 - GENERAL BIOSECURITY

4.3.4.	**Do you manage the biosecurity risk from "Sick Pens" effectively in the last 4 weeks i.e. do you fulfil at least 3 out of the following 4 requirements?**			**/4**
4.3.4.1.	Ensure that recovered pigs are not reintroduced into mainstream pens	Yes ☐	No ☐	
4.3.4.2.	Site sick pens in an appropriate separate building or if that is not possible, ensure that sick pens are placed at the end of a row so that dung etc from hospital pens is not pushed into contact with other pigs?	Yes ☐	No ☐	
4.3.4.3.	Ensure that sick pens, and any bins or holding areas used for dead pigs are cleaned and disinfected effectively to standard required *whenever they are emptied and at the start of between-batch cleaning programme?	Yes ☐	No ☐	
4.3.4.4.	Have sufficient numbers of sick pens that pens can be batch filled and emptied and fully cleaned and disinfected after completion of each batch? OR If in continuous production, have sufficient numbers of sick pens to enable their use to be alternated allowing comprehensive cleaning and disinfection of sick pens on a regular basis?	Yes ☐	No ☐	
4.3.5.	**Do you manage the biosecurity risk from "Other Animals" effectively in the last 4 weeks i.e. do you fulfil both of the following requirements?**			**/2**
4.3.5.1.	Take active measures to prevent any domestic animals (including dogs & cats) entering pig buildings or feed or bedding stores?	Yes ☐	No ☐	
4.3.5.2.	Take all efforts to minimise risk of wild birds gaining access to pig housing, or feed or bedding stores?	Yes ☐	No ☐	
4.3.6.	**Do you manage the biosecurity risk from livestock vehicles effectively the last 4 weeks i.e. do you fulfil at least 4 out of the following 6 requirements?**			**/6**
4.3.6.1.	Have a perimeter fence with gated entrances?	Yes ☐	No ☐	
4.3.6.2.	Insist on pig lorries, Deadstock collection , feed lorries, drivers always remain outside the perimeter?	Yes ☐	No ☐	
4.3.6.3.	Transport pigs between sites with your own transport and ensure vehicles are fully cleaned and disinfected to the required standard * before re-entering your site	Yes ☐	No ☐	

8

Section 4 -	GENERAL BIOSECURITY		
4.3.6.4.	Insist on pig lorries being properly cleaned and disinfected before arrival?	Yes ☐	No ☐
4.3.6.5.	Always look inside vehicle to see if it has been visibly cleaned before loading pigs?	Yes ☐	No ☐
4.3.6.6.	Ensure washing and disinfecting run-off from loading ramp drains away from your unit especially if delivery vehicle tailboard has been in contact with your loading ramp?	Yes ☐	No ☐
4.3.6.7.	Have a perimeter fence with gated entrances?	Yes ☐	No ☐
4.3.7.	**In the last 3 months did you manage biosecurity risk through effective cleaning and disinfection i.e. did you fulfil at least 4 out of the following 6 requirements *and* at least one of the 2 requirements under Monitoring of Effectiveness?**		**/6** **/2**
Pre-clean			
4.3.7.1.	Do you take out all moveable equipment for separate C and D?	Yes ☐	No ☐
4.3.7.2.	Do you soak before washing?	Yes ☐	No ☐
4.3.7.3.	Do you use a detergent?	Yes ☐	No ☐
Main clean			
4.3.7.4.	Do you rinse all surfaces after power washing?	Yes ☐	No ☐
Pre-disinfection			
4.3.7.5.	Do you allow room and all surfaces to fully dry before applying disinfectant?	Yes ☐	No ☐
Disinfection			
4.3.7.6.	Have you had verification from your vet that the disinfectant you use is effective against Salmonella?	Yes ☐	No ☐
Monitoring of effectiveness			
4.3.7.7.	Do you follow hygiene protocol devised by manufacturer and have yourself and staff regularly audited by manufacturer/vet to ensure compliance backed up by swab testing for enterobacteriaceae counts to determine effectiveness of organic matter removal?	Yes ☐	No ☐
4.3.7.8.	Has your cleaning and disinfection practice been validated as effective? (How?)	Yes ☐	No ☐
Supporting evidence requirement: ?			

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Section 5 - MANAGEMENT PRACTICE FOR EACH PRODUCTION STAGE

ANSWER THE FOLLOWING QUESTIONS FOR EACH APPLICABLE STAGE OF PRODUCTION i.e. Breeding, Weaning, Growing and Finishing

5.1 BREEDING HERD

	Indoors	Outdoors
5.1.1. No. of sows in your breeding herd based indoors or outdoors.		

5.2 WEANERS, GROWING/FINISHING

5.2.1. Which of the following best describes your production system at each production stage?

	Weaners	Growers	Finishers
All-in-all-out by site with effective C&D*	☐	☐	☐
All-in-all-out by building with effective C&D*	☐	☐	☐
All-in-all-out by room with effective C&D*	☐	☐	☐
Any All-in-all-out, without effective C&D*	☐	☐	☐
Continuous flow with effective C&D* whenever possible	☐	☐	☐
Continuous flow without effective C&D*	☐	☐	☐

* for example of effective C and D see Supporting Evidence Section 4.3.7 with links to ZNCPig 4 page self assessment

5.3 Management practice: downtime - if you answered any of the AIAO options in the question above, please complete the section below for that production stage:

5.3.1. What was the minimum time pens have been left empty for in the last six months?

	Weaners	Growers	Finishers
6+ days (or pen electrically heated for ≥ 4 hours)	☐	☐	☐
3-6 days (or pen electrically heated for 12- 24 hours)	☐	☐	☐
1-2 days, no artificial drying	☐	☐	☐
Less than 24 hours	☐	☐	☐

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Section 5 - MANAGEMENT PRACTICE FOR EACH PRODUCTION STAGE

5.4 Management practice: floor type

5.4.1. Housing system at each stage?			**Number of pig places by flooring type**					
Production stage	**Age range**	**Weight range**	**Fully slatted**	**Partially slatted**	**Solid floor – deep bedding**	**Solid floor – some bedding**	**Solid floor – no bedding**	**Outside pens**
Finishers								
Growers								
Weaners								
Sows								

Supporting evidence requirement:
Housing plan: ABP pigs requirement with stocking plan (also for below)

5.5 Management practice: Minimising stress in pigs

5.5.1. Do you always stock pigs at or under assurance scheme recommended densities? Yes ☐ No ☐

Supporting evidence requirement:
Eg House stocking record plans, sign off by AS inspection
No NC's for overstocking (Non-Compliances in Quality Assurance Schemes)

5.5.2. Within the last six months, have you ever kept any pigs >30kg back and mixed with younger ones? Yes ☐ No ☐

5.5.3. Has there been any mixing of similar-aged pigs in the last 6 months eg at housing changes or after slaughter pig selection? Yes ☐ No ☐

Supporting evidence requirement:
Eg production protocol, self declaration

5.5.4. Do you succeed in maintaining a draught-free environment for all pigs, in accordance with the Welfare guide*? Yes ☐ No ☐

Supporting evidence requirement:
No NC's for environmental deficiencies in AS inspection

5.5.5. Is the building into which weaned pigs are introduced dry and warm Yes ☐ No ☐

5.5.6. Is feed withdrawn before pigs are sent for slaughter? Yes ☐ No ☐

If yes, how long, on average, is feed withdrawn before pigs are loaded for transport? _____

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Section 6 - FEEDING PRACTICE BY PRODUCTION STAGE

6.1 Feed type currently being used or used for most recent batch

6.1.1. What is your feeding system for this particular stage? – please tick if use	**Weaner**	**Grower**	**Finisher**
Age range and/or			
Weight range			
Wet feed with pH < 4.2 Eg Use of whey	☐	☐	☐
Wet feed (pH>4.2)/meal	☐	☐	☐
Coarse ground* non-pelleted dry meal	☐	☐	☐
Fine ground non-pelleted dry meal	☐	☐	☐
Do you feed whey at this stage?	☐	☐	☐
Crude protein % in diet			
Barley, oats or beet pulp as % of diet			

6.2 Feed: products added to feed/water	**Weaner**	**Grower**	**Finisher**
Do you include acidified products in *water* during this production stage?	☐	☐	☐
If yes, which acid do you use and at what rate?			
Do you include acidified products in *feed* during this production stage?	☐	☐	☐
If yes, which acid do you use and at what rate?			
Do you include probiotics, prebiotics or other competitive exclusion products to either feed or water in this production stage?	☐	☐	☐
If yes, which product do you use?			
Have you included antibiotic products to either feed or water in this production stage within the last six months?	☐	☐	☐
If yes, which product do you use and for how long?			

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Section 6 - FEEDING PRACTICE BY PRODUCTION STAGE

Supporting evidence requirement:

Feed and medicine records?

Section 7 - PEST CONTROL

7.1.1. Which of the following best describes your approach and outcome of rodent control on your farm??

No plan in place, evidence of rodent droppings ☐

Evidence of rodent droppings, but rodent control plan followed ☐

No evidence of any rodent droppings in vicinity of pigs or feed stores and following effective* rodent control plan ☐

7.1.2. Do you follow Pest and rodent control protocol devised by a specialist pest control organisation and monitor effectiveness of approach and actively change practice to ensure no evidence of rodent droppings? Yes ☐ No ☐

Supporting evidence requirement:

*An effective rodent control plan should be in use and available for inspection. It would be expected to contain all 6 key elements outlined below:

7.1.3. Do you manage biosecurity risk through effective rodent control i.e. do you fulfil all of the following 6 requirements *and* monitor effectiveness? **/6**

7.1.3.1.	Is a baiting programme implemented regularly at key times of the year?	Yes ☐	No ☐
7.1.3.2.	Are baits topped up at least every five days	Yes ☐	No ☐
7.1.3.3.	Has a survey been carried out and baiting points sited accordingly?	Yes ☐	No ☐
7.1.3.4.	Have more than enough SECURE baiting points been used?	Yes ☐	No ☐
7.1.3.5.	Are there permanently sited empty baiting containers to get rodents used to their presence?	Yes ☐	No ☐
7.1.3.6.	Are alternative food sources rodent-proofed	Yes ☐	No ☐

7.1.4. Do other animals eg cats, dogs, other farm animals have any direct contact with pigs or enter buildings containing pigs or pig feed? Yes ☐ No ☐

7.1.5. Do birds have any direct contact with pigs or enter buildings containing pigs or pig feed? Yes ☐ No ☐

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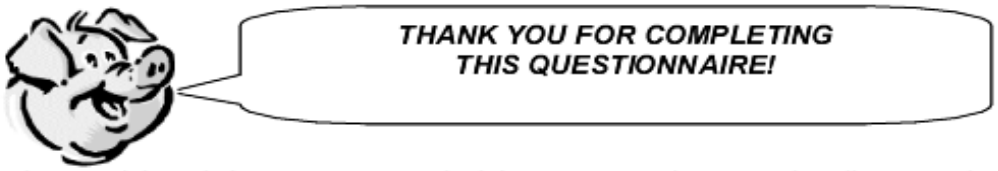
Section 8 - OVER TO YOU .....

8.1	How long did it take to complete this questionnaire?	
8.2	Which questions were the most difficult to answer?	
8.3	Were there any questions that were difficult to understand?	
8.4	Were there any questions that were duplicated?	
8.5	Were there any questions that you did not think were relevant?	

NOTES: This section is for any comments you may wish to add.



Please read through the questionnaire to check for any errors and to ensure that all questions have been answered.

Please make sure the answers are what is actually being done on the farm currently and not what it is intended to do or what was planned to be done.

Once complete, please return the questionnaire as soon as possible.

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Appendix B

MATLAB code for a multiple-roomed, fully-slatted finishing unit

```
% Multiple roomed, fully slatted. Producing a histogram of x simulations.

clear

N = 25; % Number of pigs per pen
PensPerSide = 20;
beta = 1/600; % Infections happen at rate (beta/N)SI
gamma = 1/26; % I to C
delta = 1/108; % C to I
epsilon = 1/60; % C to R
nu = 0.5; % Return to susceptibility
kappa = 4.23*10^-4; % Consumption rate
lambda = 2.25*10^4; % Shedding rate
l = 1/84; % Bacteria death rate
p = 2.30*10^-6; % Probability of susceptible pig becoming infected after consumption
alpha = 1/880000; % cross infection rate between adjacent pens
prop = 0.4; % Proportion of faeces that remains in a room
air = 1/98500000000000;
Tmax = 108; % Time spent in finisher stage (on average)

number_of_simulations = 15000;

Sresa = zeros(number_of_simulations,PensPerSide);
Eresa = zeros(number_of_simulations,PensPerSide);
Cresa = zeros(number_of_simulations,PensPerSide);
Rresa = zeros(number_of_simulations,PensPerSide);
Wresa = zeros(number_of_simulations,PensPerSide);
Sresb = zeros(number_of_simulations,PensPerSide);
```

```
Eresb = zeros(number_of_simulations,PensPerSide);
Cresb = zeros(number_of_simulations,PensPerSide);
Rresb = zeros(number_of_simulations,PensPerSide);
Wresb = zeros(number_of_simulations,PensPerSide);

Totalpigsinroom = N*(PensPerSide/4);
Totalpigsinherd = N*PensPerSide*2;

suscep_prop_initial = 0.8; infect_prop_initial = 0.15;
carrier_prop_initial = 0.05; recov_prop_initial = 0;
initial_proportions = [suscep_prop_initial infect_prop_initial; ...
                       carrier_prop_initial recov_prop_initial];

for i = 1:number_of_simulations
    i
    t = 0;
    W_D = 0; W_D1 = 0; W_D2 = 0; W_D3 = 0; W_D4 = 0;

    initial_pigs_a = mnrnd(N,initial_proportions,PensPerSide);
    Sa = initial_pigs_a(:,1); Ea = initial_pigs_a(:,2);
    Ca = initial_pigs_a(:,3); Ra = initial_pigs_a(:,4);

    initial_pigs_b = mnrnd(N,initial_proportions,PensPerSide);
    Sb = initial_pigs_b(:,1); Eb = initial_pigs_b(:,2);
    Cb = initial_pigs_b(:,3); Rb = initial_pigs_b(:,4);

 while sum(Ea+Eb+Ca+Cb+Ra+Rb) > 0 && t < Tmax
   GreatestW_D = W_D + (((1-prop)*lambda)/(air*Totalpigsinherd + l))*(sum(Ea+Eb));
   GreatestW_D1 = W_D1 + ((prop*lambda)/(kappa*Totalpigsinroom + l))*(sum(Ea(1:5))+ ...
                  sum(Eb(1:5)));
   GreatestW_D2 = W_D2 + ((prop*lambda)/(kappa*Totalpigsinroom + l))*(sum(Ea(6:10))+ ...
                  sum(Eb(6:10)));
   GreatestW_D3 = W_D3 + ((prop*lambda)/(kappa*Totalpigsinroom + l))*(sum(Ea(11:15))+ ...
                  sum(Eb(11:15)));
   GreatestW_D4 = W_D4 + ((prop*lambda)/(kappa*Totalpigsinroom + l))*(sum(Ea(16:20))+ ...
                  sum(Eb(16:20)));
   UpperTotalRate = (beta/N)*sum(Sa.*Ea) + (beta/N)*sum(Sb.*Eb) + gamma*sum(Ea) + ...
       gamma*sum(Eb) + nu*sum(Ra) + nu*sum(Rb) + delta*sum(Ca) + delta*sum(Cb) + ...
       epsilon*sum(Ca) + epsilon*sum(Cb)+ (alpha/N)*sum(Sa(2:5).*Ea(1:4)) + ...
      (alpha/N)*sum(Sa(7:10).*Ea(6:9)) + (alpha/N)*sum(Sa(12:15).*Ea(11:14)) + ...
      (alpha/N)*sum(Sa(17:PensPerSide).*Ea(16:19)) + (alpha/N)*sum(Sa(1:4).*Ea(2:5)) + ...
      (alpha/N)*sum(Sa(6:9).*Ea(7:10)) + (alpha/N)*sum(Sa(11:14).*Ea(12:15)) + ...
      (alpha/N)*sum(Sa(16:19).*Ea(17:PensPerSide)) + (alpha/N)*sum(Sb(2:5).*Eb(1:4)) + ...
      (alpha/N)*sum(Sb(7:10).*Eb(6:9)) + (alpha/N)*sum(Sb(12:15).*Eb(11:14)) + ...
      (alpha/N)*sum(Sb(17:PensPerSide).*Eb(16:19)) + (alpha/N)*sum(Sb(1:4).*Eb(2:5)) + ...
      (alpha/N)*sum(Sb(6:9).*Eb(7:10)) + (alpha/N)*sum(Sb(11:14).*Eb(12:15)) + ...
      (alpha/N)*sum(Sb(16:19).*Eb(17:PensPerSide)) + ...
      p*kappa*(sum(Sa(1:5))+sum(Sb(1:5)))*GreatestW_D1 + ...
      p*kappa*(sum(Sa(6:10))+sum(Sb(6:10)))*GreatestW_D2 + ...
```

```
 p*kappa*(sum(Sa(11:15))+sum(Sb(11:15)))*GreatestW_D3 + ...
 p*kappa*(sum(Sa(16:20))+sum(Sb(16:20)))*GreatestW_D4 + air*sum(Sa+Sb)*GreatestW_D;

while 1==1
  T = exprnd(1/UpperTotalRate);
  t = t+T;
 W_D = W_D*exp(-(air*Totalpigsinherd + l)*T) + (((1-prop)*lambda)/(air*Totalpigsinherd + l))* ...
 (sum(Ea+Eb))*(1- exp(-(air*Totalpigsinherd + l)*T));
 W_D1 = W_D1*exp(-(kappa*Totalpigsinroom + l)*T) + ((prop*lambda)/ ...
 (kappa*Totalpigsinroom + l))*(sum(Ea(1:5))+ sum(Eb(1:5)))*(1- exp(-(kappa*Totalpigsinroom + l)*T));
 W_D2 = W_D2*exp(-(kappa*Totalpigsinroom + l)*T) + ((prop*lambda)/ ...
 (kappa*Totalpigsinroom + l))*(sum(Ea(6:10))+ sum(Eb(6:10)))*(1- exp(-(kappa*Totalpigsinroom + l)*T));
 W_D3 = W_D3*exp(-(kappa*Totalpigsinroom + l)*T) + ((prop*lambda)/(kappa*Totalpigsinroom + l))* ...
 (sum(Ea(11:15))+ sum(Eb(11:15)))*(1- exp(-(kappa*Totalpigsinroom + l)*T));
 W_D4 = W_D4*exp(-(kappa*Totalpigsinroom + l)*T) + ((prop*lambda)/(kappa*Totalpigsinroom + l))* ...
 (sum(Ea(16:20))+ sum(Eb(16:20)))*(1- exp(-(kappa*Totalpigsinroom + l)*T));
TotalRate = (beta/N)*sum(Sa.*Ea) + (beta/N)*sum(Sb.*Eb) + gamma*sum(Ea) + gamma*sum(Eb) + ...
 nu*sum(Ra) + nu*sum(Rb) + delta*sum(Ca) + delta*sum(Cb) + epsilon*sum(Ca) + ...
 epsilon*sum(Cb) + (alpha/N)*sum(Sa(2:5).*Ea(1:4)) + (alpha/N)*sum(Sa(7:10).*Ea(6:9)) + ...
 (alpha/N)*sum(Sa(12:15).*Ea(11:14)) + (alpha/N)*sum(Sa(17:PensPerSide).*Ea(16:19)) + ...
 (alpha/N)*sum(Sa(1:4).*Ea(2:5)) + (alpha/N)*sum(Sa(6:9).*Ea(7:10)) + ...
 (alpha/N)*sum(Sa(11:14).*Ea(12:15)) + (alpha/N)*sum(Sa(16:19).*Ea(17:PensPerSide)) + ...
 (alpha/N)*sum(Sb(2:5).*Eb(1:4)) + (alpha/N)*sum(Sb(7:10).*Eb(6:9)) + ...
 (alpha/N)*sum(Sb(12:15).*Eb(11:14)) + (alpha/N)*sum(Sb(17:PensPerSide).*Eb(16:19)) + ...
 (alpha/N)*sum(Sb(1:4).*Eb(2:5)) + (alpha/N)*sum(Sb(6:9).*Eb(7:10)) + ...
 (alpha/N)*sum(Sb(11:14).*Eb(12:15)) + (alpha/N)*sum(Sb(16:19).*Eb(17:PensPerSide)) + ...
  p*kappa*sum(Sa(1:5))*W_D1 + p*kappa*sum(Sb(1:5))*W_D1 + p*kappa*sum(Sa(6:10))*W_D2 + ...
  p*kappa*sum(Sb(6:10))*W_D2 + p*kappa*sum(Sa(11:15))*W_D3 + p*kappa*sum(Sb(11:15))*W_D3 + ...
  p*kappa*sum(Sa(16:20))*W_D4 + p*kappa*sum(Sb(16:20))*W_D4 + air*sum(Sa+Sb)*W_D;

    U = rand;
    if U > TotalRate/UpperTotalRate
       break
    end
end

 V = rand*TotalRate;

 cumulative_rate = 0;
 for group = 1:PensPerSide
 cumulative_rate = cumulative_rate + (beta/N)*Sa(group).*Ea(group);
 if V < cumulative_rate
    Sa(group) = Sa(group)-1;
    Ea(group) = Ea(group)+1;
    break
 end
 cumulative_rate = cumulative_rate + nu*Ra(group);
 if V < cumulative_rate
    Sa(group) = Sa(group)+1;
```

```
    Ra(group) = Ra(group)-1;
    break
end
cumulative_rate = cumulative_rate + air*Sa(group)*W_D;
if V < cumulative_rate
    Sa(group) = Sa(group)-1;
    Ea(group) = Ea(group)+1;
    break
end
cumulative_rate = cumulative_rate + delta*Ca(group);
if V < cumulative_rate
    Ea(group) = Ea(group)+1;
    Ca(group) = Ca(group)-1;
    break
end
cumulative_rate = cumulative_rate + gamma*Ea(group);
if V < cumulative_rate
    Ea(group) = Ea(group)-1;
    Ca(group) = Ca(group)+1;
    break
end
cumulative_rate = cumulative_rate + epsilon*Ca(group);
if V < cumulative_rate
    Ca(group) = Ca(group)-1;
    Ra(group) = Ra(group)+1;
    break
end
end

if V < cumulative_rate
    continue
end

for group = 1:4
cumulative_rate = cumulative_rate + (alpha/N)*(Sa(group+1).*Ea(group));
if V < cumulative_rate
    Sa(group+1) = Sa(group+1)-1;
    Ea(group+1) = Ea(group+1)+1;
    break
end
cumulative_rate = cumulative_rate + (alpha/N)*(Sa(group).*Ea(group+1));
if V < cumulative_rate
    Sa(group) = Sa(group)-1;
    Ea(group) = Ea(group)+1;
    break
end
end

if V < cumulative_rate
```

```
    continue
end

for group = 1:5
cumulative_rate = cumulative_rate + p*kappa*Sa(group)*W_D1;
if V < cumulative_rate
    Sa(group) = Sa(group)-1;
    Ea(group) = Ea(group)+1;
    break
end
end

if V < cumulative_rate
    continue
end

for group = 6:9
cumulative_rate = cumulative_rate + (alpha/N)*(Sa(group+1).*Ea(group));
if V < cumulative_rate
    Sa(group+1) = Sa(group+1)-1;
    Ea(group+1) = Ea(group+1)+1;
    break
end
cumulative_rate = cumulative_rate + (alpha/N)*(Sa(group).*Ea(group+1));
if V < cumulative_rate
    Sa(group) = Sa(group)-1;
    Ea(group) = Ea(group)+1;
    break
end
end

if V < cumulative_rate
    continue
end

for group = 6:10
cumulative_rate = cumulative_rate + p*kappa*Sa(group)*W_D2;
if V < cumulative_rate
    Sa(group) = Sa(group)-1;
    Ea(group) = Ea(group)+1;
    break
end
end

if V < cumulative_rate
    continue
end

for group = 11:14
```

```
cumulative_rate = cumulative_rate + (alpha/N)*(Sa(group+1).*Ea(group));
if V < cumulative_rate
    Sa(group+1) = Sa(group+1)-1;
    Ea(group+1) = Ea(group+1)+1;
    break
end
cumulative_rate = cumulative_rate + (alpha/N)*(Sa(group).*Ea(group+1));
if V < cumulative_rate
    Sa(group) = Sa(group)-1;
    Ea(group) = Ea(group)+1;
    break
end
end

if V < cumulative_rate
    continue
end

for group = 11:15
cumulative_rate = cumulative_rate + p*kappa*Sa(group)*W_D3;
if V < cumulative_rate
    Sa(group) = Sa(group)-1;
    Ea(group) = Ea(group)+1;
    break
end
end

if V < cumulative_rate
    continue
end
for group = 16:PensPerSide-1
cumulative_rate = cumulative_rate + (alpha/N)*(Sa(group+1).*Ea(group));
if V < cumulative_rate
    Sa(group+1) = Sa(group+1)-1;
    Ea(group+1) = Ea(group+1)+1;
    break
end
cumulative_rate = cumulative_rate + (alpha/N)*(Sa(group).*Ea(group+1));
if V < cumulative_rate
    Sa(group) = Sa(group)-1;
    Ea(group) = Ea(group)+1;
    break
end
end

if V < cumulative_rate
    continue
end
```

```
 for group = 16:PensPerSide
 cumulative_rate = cumulative_rate + p*kappa*Sa(group)*W_D4;
 if V < cumulative_rate
     Sa(group) = Sa(group)-1;
     Ea(group) = Ea(group)+1;
     break
 end
 end

 if V < cumulative_rate
     continue
 end

for group = 1:PensPerSide
cumulative_rate = cumulative_rate + (beta/N)*Sb(group).*Eb(group);
if V < cumulative_rate
     Sb(group) = Sb(group)-1;
     Eb(group) = Eb(group)+1;
     break
end
cumulative_rate = cumulative_rate + air*Sb(group)*W_D;
 if V < cumulative_rate
     Sb(group) = Sb(group)-1;
     Eb(group) = Eb(group)+1;
     break
end
cumulative_rate = cumulative_rate + nu*Rb(group);
 if V < cumulative_rate
     Sb(group) = Sb(group)+1;
     Rb(group) = Rb(group)-1;
     break
end
cumulative_rate = cumulative_rate + delta*Cb(group);
 if V < cumulative_rate
     Eb(group) = Eb(group)+1;
     Cb(group) = Cb(group)-1;
     break
end
cumulative_rate = cumulative_rate + gamma*Eb(group);
 if V < cumulative_rate
     Eb(group) = Eb(group)-1;
     Cb(group) = Cb(group)+1;
     break
end
cumulative_rate = cumulative_rate + epsilon*Cb(group);
 if V < cumulative_rate
     Cb(group) = Cb(group)-1;
     Rb(group) = Rb(group)+1;
     break
```

```
end
end

if V < cumulative_rate
   continue
end

for group = 1:4
cumulative_rate = cumulative_rate + (alpha/N)*(Sb(group+1).*Eb(group));
 if V < cumulative_rate
    Sb(group+1) = Sb(group+1)-1;
    Eb(group+1) = Eb(group+1)+1;
    break
end
cumulative_rate = cumulative_rate + (alpha/N)*(Sb(group).*Eb(group+1));
 if V < cumulative_rate
    Sb(group) = Sb(group)-1;
    Eb(group) = Eb(group)+1;
    break
end
end

 if V < cumulative_rate
   continue
end

for group = 1:5
cumulative_rate = cumulative_rate + p*kappa*Sb(group)*W_D1;
 if V < cumulative_rate
    Sb(group) = Sb(group)-1;
    Eb(group) = Eb(group)+1;
    break
end
end

 if V < cumulative_rate
    continue
end

for group = 6:9
cumulative_rate = cumulative_rate + (alpha/N)*(Sb(group+1).*Eb(group));
 if V < cumulative_rate
    Sb(group+1) = Sb(group+1)-1;
    Eb(group+1) = Eb(group+1)+1;
    break
end
cumulative_rate = cumulative_rate + (alpha/N)*(Sb(group).*Eb(group+1));
 if V < cumulative_rate
    Sb(group) = Sb(group)-1;
```

```
    Eb(group) = Eb(group)+1;
    break
end
end

 if V < cumulative_rate
    continue
 end

for group = 6:10
cumulative_rate = cumulative_rate + p*kappa*Sb(group)*W_D2;
 if V < cumulative_rate
    Sb(group) = Sb(group)-1;
    Eb(group) = Eb(group)+1;
    break
end
end

 if V < cumulative_rate
    continue
end

for group = 11:14
cumulative_rate = cumulative_rate + (alpha/N)*(Sb(group+1).*Eb(group));
 if V < cumulative_rate
    Sb(group+1) = Sb(group+1)-1;
    Eb(group+1) = Eb(group+1)+1;
    break
end
cumulative_rate = cumulative_rate + (alpha/N)*(Sb(group).*Eb(group+1));
 if V < cumulative_rate
    Sb(group) = Sb(group)-1;
    Eb(group) = Eb(group)+1;
    break
end
end

 if V < cumulative_rate
    continue
end

for group = 11:15
cumulative_rate = cumulative_rate + p*kappa*Sb(group)*W_D3;
 if V < cumulative_rate
    Sb(group) = Sb(group)-1;
    Eb(group) = Eb(group)+1;
    break
end
end
```

```
        if V < cumulative_rate
            continue
        end

        for group = 16:PensPerSide-1
        cumulative_rate = cumulative_rate + (alpha/N)*(Sb(group+1).*Eb(group));
        if V < cumulative_rate
            Sb(group+1) = Sb(group+1)-1;
            Eb(group+1) = Eb(group+1)+1;
            break
        end
        cumulative_rate = cumulative_rate + (alpha/N)*(Sb(group).*Eb(group+1));
        if V < cumulative_rate
            Sb(group) = Sb(group)-1;
            Eb(group) = Eb(group)+1;
            break
        end
        end

        if V < cumulative_rate
            continue
        end

        for group = 16:PensPerSide
        cumulative_rate = cumulative_rate + p*kappa*Sb(group)*W_D4;
        if V < cumulative_rate
            Sb(group) = Sb(group)-1;
            Eb(group) = Eb(group)+1;
            break
        end
        end

    end

FinalWgen(i) = W_D;
FinalW1(i) = W_D1;
FinalW2(i) = W_D2;
FinalW3(i) = W_D3;
FinalW4(i) = W_D4;

Sresa(i,:)= Sa; Eresa(i,:)= Ea; Cresa(i,:)= Ca; Rresa(i,:)= Ra;
Sresb(i,:)= Sb; Eresb(i,:)= Eb; Cresb(i,:)= Cb; Rresb(i,:)= Rb;

if TotalRate > UpperTotalRate
    error('myApp:argChk', 'Total rate too big')
end
end
Sresult = sum(Sresa') + sum(Sresb'); Eresult = sum(Eresa') + sum(Eresb');
```

```
Cresult = sum(Cresa') + sum(Cresb'); Rresult = sum(Rresa') + sum(Rresb');

Total = Sresult + Eresult + Cresult + Rresult;

PrevalenceE = (Eresult/Total)*100
PrevalenceEandC = ((Eresult + Cresult)/Total)*100

figure
hold on
subplot(4,1,1); hist(Sresult)
title('Susceptibles')
subplot(4,1,2); hist(Eresult)
title('Infectious')
subplot(4,1,3); hist(Cresult)
title('Carrier')
subplot(4,1,4); hist(Rresult)
title('Recovered')
xlabel('Number of pigs')
ylabel('Number of simulations')

figure
hold on
hist(FinalWgen)
title('Bacteria')
xlabel('Amount of bacteria')
ylabel('Number of simulations')

figure
hold on
subplot(4,1,1); hist(FinalW1)
title('Bacteria Room 1')
subplot(4,1,2); hist(FinalW2)
title('Bacteria Room 2')
subplot(4,1,3); hist(FinalW3)
title('Bacteria Room 3')
subplot(4,1,4); hist(FinalW4)
title('Bacteria Room 4')
xlabel('Amount of bacteria')
ylabel('Number of simulations')
```

Appendix C

MATLAB code for a solid-floored finishing unit

```
% Trajectories code for a solid unit

clear

N = 25; % Number of pigs per pen
PensPerSide = 20;
beta = 1/600; % Infections happen at rate (beta/N)SI
gamma = 1/26; % Recovery happens at rate (gamma I)
delta = 1/108; % Carrier to Infectious
epsilon = 1/60; % Carrier to Recovered
nu = 0.5; % Return to susceptibility
kappa = 3.17*10^-5; % Consumption rate
lambda = 2.25*10^4; % Shedding rate
l = 1/84; % Bacteria death rate
p = 2.30*10^-6; % probability of a susceptible pig becoming infected after consumption
alpha = 1/880000; % cross infection rate between adjacent pens
air = 1/98500000000000;
q = 0.1; %Proportion of bacteria left present after scraping
Tmax = 108; % Time spent in finishing

Vectorsize = 10000;
Sa = zeros(PensPerSide,Vectorsize);
Ea = zeros(PensPerSide,Vectorsize);
Ca = zeros(PensPerSide,Vectorsize);
Ra = zeros(PensPerSide,Vectorsize);
Sb = zeros(PensPerSide,Vectorsize);
Eb = zeros(PensPerSide,Vectorsize);
Cb = zeros(PensPerSide,Vectorsize);
Rb = zeros(PensPerSide,Vectorsize);
W_D = zeros(1,Vectorsize);
T = zeros(1,Vectorsize);
```

```
Totalpigsinherd = N*PensPerSide*2;

suscep_prop_initial = 0.8; infect_prop_initial = 0.15;
carrier_prop_initial = 0.05; recov_prop_initial = 0;
initial_proportions = [suscep_prop_initial infect_prop_initial; ...
                       carrier_prop_initial recov_prop_initial];

initial_pigs_a=mnrnd(N,initial_proportions,PensPerSide);
Sa(:,1) = initial_pigs_a(:,1); Ea(:,1) = initial_pigs_a(:,2);
Ca(:,1) = initial_pigs_a(:,3); Ra(:,1) = initial_pigs_a(:,4);

initial_pigs_b=mnrnd(N,initial_proportions,PensPerSide);
Sb(:,1) = initial_pigs_b(:,1); Eb(:,1) = initial_pigs_b(:,2);
Cb(:,1) = initial_pigs_b(:,3); Rb(:,1) = initial_pigs_b(:,4);

i=0;

 while sum(Ea(:,i+1)+Eb(:,i+1)+Ca(:,i+1)+Cb(:,i+1)+Ra(:,i+1)+Rb(:,i+1)) > 0 && T(i+1) < Tmax
       i=i+1;

    GreatestW_D = W_D(i) + (lambda/(kappa*Totalpigsinherd + air*Totalpigsinherd + l))* ...
                  (sum(Ea(:,i))+ sum(Eb(:,i)));
    UpperTotalRate = (beta/N)*sum(Sa(:,i).*Ea(:,i)) + (beta/N)*sum(Sb(:,i).*Eb(:,i)) + ...
        gamma*sum(Ea(:,i)) + gamma*sum(Eb(:,i)) + nu*sum(Ra(:,i)) + nu*sum(Rb(:,i)) + ...
        delta*sum(Ca(:,i)) + delta*sum(Cb(:,i)) + epsilon*sum(Ca(:,i)) + epsilon*sum(Cb(:,i)) + ...
        p*kappa*sum(Sa(:,i))*GreatestW_D + p*kappa*sum(Sb(:,i))*GreatestW_D + ...
        (alpha/N)*sum(Sa(2:PensPerSide,i).*Ea(1:(PensPerSide-1),i)) + ...
        (alpha/N)*sum(Sa(1:(PensPerSide-1),i).*Ea(2:PensPerSide,i)) + ...
        (alpha/N)*sum(Sb(2:PensPerSide,i).*Eb(1:(PensPerSide-1),i)) + ...
        (alpha/N)*sum(Sb(1:(PensPerSide-1),i).*Eb(2:PensPerSide,i)) + ...
        air*sum(Sa(:,i))*GreatestW_D + air*sum(Sb(:,i))*GreatestW_D;

      W_D_now = W_D(i);
      Current_time = T(i);
      Last_week_boundary = floor(T(i)/7) * 7;

      while 1==1
         t = exprnd(1/UpperTotalRate);
         Proposed_event_time = Current_time + t;

         while Proposed_event_time > Last_week_boundary + 7

           Next_week_boundary = Last_week_boundary + 7;
           Time_before_cleaning = Next_week_boundary - Current_time;

          W_D_now = q*(W_D_now*exp(-(kappa*Totalpigsinherd + air*Totalpigsinherd + l)* ...
                (Time_before_cleaning)) + (lambda/(kappa*Totalpigsinherd + air*Totalpigsinherd + l))* ...
                (sum(Ea(:,i))+ sum(Eb(:,i)))*(1- exp(-(kappa*Totalpigsinherd + air*Totalpigsinherd + l)* ...
                (Time_before_cleaning))));
```

```
    GreatestW_D = W_D_now + (lambda/(kappa*Totalpigsinherd + air*Totalpigsinherd + l))* ...
                  (sum(Ea(:,i))+ sum(Eb(:,i)));
     UpperTotalRate = (beta/N)*sum(Sa(:,i).*Ea(:,i)) + (beta/N)*sum(Sb(:,i).*Eb(:,i)) + ...
        gamma*sum(Ea(:,i)) + gamma*sum(Eb(:,i)) + nu*sum(Ra(:,i)) + nu*sum(Rb(:,i)) + ...
        delta*sum(Ca(:,i)) + delta*sum(Cb(:,i)) + epsilon*sum(Ca(:,i)) + epsilon*sum(Cb(:,i))+ ...
        p*kappa*sum(Sa(:,i))*GreatestW_D + p*kappa*sum(Sb(:,i))*GreatestW_D + ...
        (alpha/N)*sum(Sa(2:PensPerSide,i).*Ea(1:(PensPerSide-1),i)) + ...
        (alpha/N)*sum(Sa(1:(PensPerSide-1),i).*Ea(2:PensPerSide,i)) + ...
        (alpha/N)*sum(Sb(2:PensPerSide,i).*Eb(1:(PensPerSide-1),i)) + ...
        (alpha/N)*sum(Sb(1:(PensPerSide-1),i).*Eb(2:PensPerSide,i)) + ...
        air*sum(Sa(:,i))*GreatestW_D + air*sum(Sb(:,i))*GreatestW_D;

        Current_time = Next_week_boundary;

        t = exprnd(1/UpperTotalRate);
        Proposed_event_time = Current_time + t;

        Last_week_boundary = Next_week_boundary;
      end

  Time_after_cleaning = Proposed_event_time - Last_week_boundary;
W_D_now = W_D_now*exp(-(kappa*Totalpigsinherd + air*Totalpigsinherd + l)*Time_after_cleaning) + ...
    (lambda/(kappa*Totalpigsinherd + air*Totalpigsinherd + l))*(sum(Ea(:,i))+ sum(Eb(:,i)))* ...
    (1- exp(-(kappa*Totalpigsinherd + air*Totalpigsinherd + l)*Time_after_cleaning));

TotalRate = (beta/N)*sum(Sa(:,i).*Ea(:,i)) + (beta/N)*sum(Sb(:,i).*Eb(:,i)) + gamma*sum(Ea(:,i)) + ...
    gamma*sum(Eb(:,i)) + nu*sum(Ra(:,i)) + nu*sum(Rb(:,i)) + delta*sum(Ca(:,i)) + ...
    delta*sum(Cb(:,i)) + epsilon*sum(Ca(:,i)) + epsilon*sum(Cb(:,i)) + ...
    p*kappa*sum(Sa(:,i))*W_D_now + p*kappa*sum(Sb(:,i))*W_D_now + ...
    (alpha/N)*sum(Sa(2:PensPerSide,i).*Ea(1:(PensPerSide-1),i)) + ...
    (alpha/N)*sum(Sa(1:(PensPerSide-1),i).*Ea(2:PensPerSide,i)) + ...
    (alpha/N)*sum(Sb(2:PensPerSide,i).*Eb(1:(PensPerSide-1),i)) + ...
    (alpha/N)*sum(Sb(1:(PensPerSide-1),i).*Eb(2:PensPerSide,i)) + ...
    air*sum(Sa(:,i))*W_D_now + air*sum(Sb(:,i))*W_D_now;

  U = rand;
  if U < TotalRate/UpperTotalRate
      break
   end
 end

 W_D(i+1) = W_D_now;
 T(i+1) = Proposed_event_time;

  V = rand*TotalRate;

  Sa(:,i+1) = Sa(:,i); Ea(:,i+1) = Ea(:,i);
  Ca(:,i+1) = Ca(:,i); Ra(:,i+1) = Ra(:,i);
  Sb(:,i+1) = Sb(:,i); Eb(:,i+1) = Eb(:,i);
```

```
Cb(:,i+1) = Cb(:,i); Rb(:,i+1) = Rb(:,i);

cumulative_rate = 0;
for group = 1:PensPerSide
    cumulative_rate = cumulative_rate + (beta/N)*Sa(group,i).*Ea(group,i);
if V < cumulative_rate
    Sa(group,i+1) = Sa(group,i)-1;
    Ea(group,i+1) = Ea(group,i)+1;
    break
end
cumulative_rate = cumulative_rate + p*kappa*Sa(group,i)*W_D(i+1);
if V < cumulative_rate
    Sa(group,i+1) = Sa(group,i)-1;
    Ea(group,i+1) = Ea(group,i)+1;
    break
end
cumulative_rate = cumulative_rate + nu*Ra(group,i);
if V < cumulative_rate
    Sa(group,i+1) = Sa(group,i)+1;
    Ra(group,i+1) = Ra(group,i)-1;
    break
end
cumulative_rate = cumulative_rate + delta*Ca(group,i);
if V < cumulative_rate
    Ea(group,i+1) = Ea(group,i)+1;
    Ca(group,i+1) = Ca(group,i)-1;
    break
end
cumulative_rate = cumulative_rate + gamma*Ea(group,i);
if V < cumulative_rate
    Ea(group,i+1) = Ea(group,i)-1;
    Ca(group,i+1) = Ca(group,i)+1;
    break
end
cumulative_rate = cumulative_rate + epsilon*Ca(group,i);
if V < cumulative_rate
    Ca(group,i+1) = Ca(group,i)-1;
    Ra(group,i+1) = Ra(group,i)+1;
    break
end
cumulative_rate = cumulative_rate + air*Sa(group,i)*W_D(i+1);
if V < cumulative_rate
    Sa(group,i+1) = Sa(group,i)-1;
    Ea(group,i+1) = Ea(group,i)+1;
    break
end

if group == PensPerSide
   break
```

```
 end

 cumulative_rate = cumulative_rate + (alpha/N)*(Sa(group+1,i).*Ea(group,i));
 if V < cumulative_rate
     Sa(group+1,i+1) = Sa(group+1,i)-1;
     Ea(group+1,i+1) = Ea(group+1,i)+1;
     break
 end
 cumulative_rate = cumulative_rate + (alpha/N)*(Sa(group,i).*Ea(group+1,i));
 if V < cumulative_rate
 Sa(group,i+1) = Sa(group,i)-1;
 Ea(group,i+1) = Ea(group,i)+1;
 break
 end

 end

if V > cumulative_rate
for group = 1:PensPerSide
    cumulative_rate = cumulative_rate + (beta/N)*Sb(group,i).*Eb(group,i);
if V < cumulative_rate
     Sb(group,i+1) = Sb(group,i)-1;
     Eb(group,i+1) = Eb(group,i)+1;
     break
end
cumulative_rate = cumulative_rate + p*kappa*Sb(group,i)*W_D(i+1);
 if V < cumulative_rate
     Sb(group,i+1) = Sb(group,i)-1;
     Eb(group,i+1) = Eb(group,i)+1;
     break
 end
 cumulative_rate = cumulative_rate + nu*Rb(group,i);
 if V < cumulative_rate
     Sb(group,i+1) = Sb(group,i)+1;
     Rb(group,i+1) = Rb(group,i)-1;
     break
 end
 cumulative_rate = cumulative_rate + delta*Cb(group,i);
 if V < cumulative_rate
     Eb(group,i+1) = Eb(group,i)+1;
     Cb(group,i+1) = Cb(group,i)-1;
     break
 end
 cumulative_rate = cumulative_rate + gamma*Eb(group,i);
 if V < cumulative_rate
     Eb(group,i+1) = Eb(group,i)-1;
     Cb(group,i+1) = Cb(group,i)+1;
     break
 end
```

```
        cumulative_rate = cumulative_rate + epsilon*Cb(group,i);
        if V < cumulative_rate
            Cb(group,i+1) = Cb(group,i)-1;
            Rb(group,i+1) = Rb(group,i)+1;
            break
        end
        cumulative_rate = cumulative_rate + air*Sb(group,i)*W_D(i+1);
        if V < cumulative_rate
            Sb(group,i+1) = Sb(group,i)-1;
            Eb(group,i+1) = Eb(group,i)+1;
            break
        end

         if group==PensPerSide
            break
        end
        cumulative_rate = cumulative_rate + (alpha/N)*(Sb(group+1,i).*Eb(group,i));
        if V < cumulative_rate
            Sb(group+1,i+1) = Sb(group+1,i)-1;
            Eb(group+1,i+1) = Eb(group+1,i)+1;
            break
        end
        cumulative_rate = cumulative_rate + (alpha/N)*(Sb(group,i).*Eb(group+1,i));
        if V < cumulative_rate
            Sb(group,i+1) = Sb(group,i)-1;
            Eb(group,i+1) = Eb(group,i)+1;
            break
       end
    end
  end
end

sumS = sum(Sa(:,1:i)+Sb(:,1:i)); sumE = sum(Ea(:,1:i)+Eb(:,1:i));
sumC = sum(Ca(:,1:i)+Cb(:,1:i)); sumR = sum(Ra(:,1:i)+Rb(:,1:i));
Prevalence= ((sumE(end)+sumC(end))/(sumS(end)+sumE(end)+sumC(end)+sumR(end)))*100

figure
hold on
plot(T(1:i),sumS); plot(T(1:i),sumE,'r');
plot(T(1:i),sumC,'g'); plot(T(1:i),sumR,'m');
legend('S','I','C','R')
xlabel('Time')
ylabel('Number of pigs')

figure
stairs(T(1:i),W_D(1:i),'k')
xlabel('Time')
ylabel('Amount of bacteria')
```